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Fatal infections in primary immunodeficiencies – how to setup a systematic review

MASTERARBEIT

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Contents

1. Abstract

Background: A systematic review is a highly authoritative study design. It is aimed at synthesizing and analysing all available data from literature qualitatively or quantitatively using systematic methods. Primary immunodeficiency (PID) is a heterogenous group of diseases that are often characterized by increased susceptibility to infections and infectious complications. In cases of severe infections in the general population, the prevalence of PID is much higher than previously thought. Diagnostic delay leads to preventable complications.

Objective: To explore and identify challenges in the execution of a systematic review based on a scoping review to form the basis for the planning and execution of a doctoral thesis with the goal of publishing a systematic review on fatal infections in PID.

Methods: Embase, Medline, Pubmed and Scopus were searched for the combination of fatal infection and various PID search terms on 5 February 2018. The methods used for the various steps were evaluated using the PRISMA-Protocol checklist.

Results: Of 2557 articles, 129 were included in the synthesis, yielding 225 individual fatal cases with a total of 375 occurrences of 87 distinct pathogens. These cases were associated with 63 distinct genetic diagnoses of PID.

Discussion: Taking into account the available publications on lethal infections in patients with PID, we are confident to be able to provide a comprehensive and well documented overview assessing the genetic causes of lethal infections. This allows us to suggest genetic candidates to screen for when managing patients with severe infections and to highlight areas requiring further research. The preliminary results of this scoping review may well be useful for the clinician even now but would benefit from validation by comparison to patient registry data. A systematic mapping review was identified as a possible alternative methodology for this review.

2. List of abbreviations

ADA	Adenosine deaminase
BCG	Bacillus Calmette-Guérin
CARE	CAse REport (CARE) guidelines checklist
CoNS	Coagulase-negative Staphylococci (not S. aureus)
CoxV	Coxsackievirus
CVID	Common variable immunodeficiency
EBV	Epstein-Barr virus
FLUBV	Influenza B virus
GBS	Group B streptococci (S. agalacticae)
GNB	Gram-negative bacteria
GPB	Gram-positive bacteria
H1N1	Influenza A virus subtype H1N1
HAdV	Human adenovirus
HBV	Hepatitis B virus
HCMV	Human cytomegalovirus
HCV	Hepatitis C virus
HHV6	Human herpesvirus 6
HPIV-3	Human parainfluenza virus III
HPV	Human papillomavirus
HRSV	Human respiratory syncytial virus
HSCT	Haematopoietic stem cell transplantation
HSV	Herpes simplex virus
JaCaV	Jamestown canyon virus
JCPyV	John Cunningham polyomavirus
MAC	Mycobacterium avium complex
MRSA	Methicillin-resistant S. aureus
NoV	Norovirus
PID	Primary immunodeficiency
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PVB19	Human parvovirus B19
RCT	Randomized controlled trial
SCID	Severe combined immunodeficiency
TB	Mycobacterium tuberculosis
VZV	Varicella zoster virus

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4. Introduction

4.1. Systematic Reviews

Due to the explosion in the number of publications in the last few decades it has become a mere necessity to summarize and analyse previously published knowledge.[1] Since evidence-based medicine has put this type of publication at the top of its evidence pyramid, it has become even more attractive to write and publish a systematic review.[2] This has unfortunately also led to the publication of numerous unnecessary, misleading, and/or conflicted systematic reviews.[3]

In other words, systematic reviews play an important but challenging role in the facilitation of knowledge transfer from theory to practice.[4] While the strongest proof for causality stems from the methodology used in randomized controlled trials (RCTs), research using this study design has not been done for every valuable research question.[5] A systematic review should always include the best available evidence, but for many rare diseases the strongest evidence available consists of case reports or case series.[6,7]

In 2009 the PRISMA statement has been published to guide authors in the process of preparing, conducting and writing a systematic review or meta-analysis.[8] A meta-analysis may be done in a systematic review or by itself to quantitatively integrate and summarize results from multiple studies using statistical analysis.[9] The key characteristics of a systematic review as defined by the PRIMSA statement are as follows:

1) a clearly stated set of objectives with an explicit, reproducible methodology
2) a systematic search that attempts to identify all studies that would meet the eligibility criteria
3) an assessment of the validity of the findings of the included studies, for example through the assessment of risk of bias
4) systematic presentation, and synthesis, of the characteristics and findings of the included studies

When conducting a systematic review, it is important to work with a protocol that sets out the exact steps and chosen criteria for each step. A manual has also been written to guide authors in preparing such a protocol.[10] It is currently considered best-practice to publish this protocol before data extraction has begun, either in a journal or in a registry dedicated to the sole purpose of holding systematic review protocols.[11]

The focus of systematic reviews has often been on healthcare interventions, but with some methodological adaptations, systematic reviews can be used to answer many other types of research questions .[12,13]

4.2. Primary immunodeficiency (PID)

PID is a heterogeneous group of diseases that is characterized by an inborn error of the immune system.[14] This includes conditions linked to increased susceptibility to infections, as well as non-infectious diseases such as allergies, malignancies and autoimmune diseases.[15] The first international classification of these diseases, published in 1968, distinguished just 11 entities.[16] [16]With the arrival of modern gene technology this number has increased substantially: The 2017 classification distinguishes more than 300 conditions.[17]

PIDs appear to be rare, but are actually more common than previously thought.[18,19,20] A child with severe combined immunodeficiency (SCID) is likely to die from infection in its first year of life unless haematopoietic stem cell transplantation is performed.[21] Many somewhat less severe PIDs exist, some characterized by syndromic features, others by agammaglobulinemia or B cell dysfunction, yet others by immune dysregulation or phagocyte dysfunction.[17] While most PIDs are characterized by increased susceptibility to infectious complications, in some PIDs this susceptibility is limited to a small number of specific infectious agents.[20,22,23,24]

Currently the only curative treatment for most PIDs is a complete replacement of the cellular immune system by haematopoietic stem cell transplantation, while patients with other PIDs can benefit from more specific approaches, e.g. gene therapy, targeted treatment and enzyme replacement gene therapy for ADA-deficiency.[21,25] Transplantation is a challenging procedure that poses additional risk to die from infections until the new immune system has fully engrafted.[26] Finally it is important to stress that the shorter the diagnostic delay, the more infectious and non-infectious complications may be avoided.[27,28,29]

4.3. Infections in PID

Despite substantial global progress in reducing childhood mortality, infections and congenital anomalies remain amongst the leading causes of death in children under 5 years.[30] Rare genetic variants causing primary immunodeficiencies (PIDs) may underlie lethal infections.[31,24] Although PIDs are rare in the general population, the proportion of PIDs amongst young children with invasive infections reaches up to 26%.[32,33] Host DNA sequencing has been proposed as a diagnostic procedure, also for previously heathy children presenting with unusually severe or fatal sepsis.[33]

Genetic testing in most laboratories may not be fast enough to be able to help in clinical decisions in a severely ill patient.[34] Nevertheless, genetic testing is highly relevant to survivors and affected families.[35] Nowadays, most laboratories offer either chromosomal microarray analysis together with targeted sequencing panels or whole exome sequencing in patients with suspected PID with a broad differential diagnosis.[36] Targeted gene sequencing panels are useful tools for analysing specific genes or gene regions and will give faster results, better resolution and more manageable data sets compared to broader approaches such as whole exome or whole genome sequencing.[37] Either way, it is important for the clinician to be aware of which genes have been analysed and whether the analysed set of genes contains all clinically relevant candidates.

When facing a patient with unusually severe or frequent infections, or infections in unusual locations or with unusual pathogens, the treating physician may raise suspicion for PID.[38] The current increase of data on different PIDs has made it difficult for physicians, to have a complete overview of the differential diagnosis associated with bacterial, viral or fungal sepsis. The constellation of infections in the history of the patient may give valuable clues if it can be compared to previous cases with PID. Even more so when fatal infections have occurred in the family history.[29]

4.4. Objectives

The objective of this master thesis is:

- to explore the steps involved in setting up a systematic review and to identify the challenges involved in each step.
- to identify concepts used in the literature to allow for the adjustment of the search method in the planned systematic review. The systematic review as described in this thesis is thereby conceived as a preliminary “scoping” stage of a systematic literature review on fatal infections in PIDs.
- to reflect on the appropriateness of the used method and to recommend considerations for similar studies in the future.

The results of this work will form the basis of a doctoral thesis, with the ultimate goal of publishing a systematic review of fatal infections in PID.

5. Methods

5.1. Search strategy and data sources

A general search strategy was developed as described below. Assistance was provided in the execution of the search query by a librarian, as recommended by experts in the field.[39] The exact search terms used for each consulted database are available in Appendix A-D. The following databases were consulted: Embase, Medline, Pubmed and Scopus.

If an included case report or a corresponding author of an included case identified another published article with additional details on the same patient, this article's full text was consulted and added to the pool.

5.1.1. *General search strategy*

Include any article that mentions in the title or abstract the word "*recurrent*", "*fatal*", or one of 10 synonyms of the latter, <u>in combination</u> with the word "*infection*", "*inflammat**" or one of several names for localised infection. Also include any article tagged with appropriate keywords if available: "infection", "inflammation", "respiratory insufficiency", "respiratory failure", or that mentions "respiratory failure" in the title or abstract. Exclude from the resulting pool any article that is not tagged with "fatality", "cause of death", "autopsy", "mortality" or "death". Of the remaining articles only keep those that mention one of 349 gene names related to PID or the term "PID" (see Appendix E for the complete list) in the title or abstract. Use the database filters to select only articles related to humans, exclude animal studies and articles tagged with the keyword "HIV" or "HIV infection". Keep only articles written in English, French, German or Italian.

5.2. Selection of articles based on title and abstract and selection criteria

The search results were provided by the librarian as a reference collection file for EndNote reference manager X7 by Clarivate Analytics. Automatic disposal of duplicate articles was performed in this program. After this, a subset of articles (all those author's name starting on the letter A) was screened on relevance based on title and abstract by both MK and KE and results were compared to check for consistency. Differences were discussed in a peer group meeting and based on the discussion it was decided to exclude any article that deals primarily with cystic fibrosis.

The remaining articles were screened by either MK or KE into 3 categories: *relevant*, *not relevant* or *unsure*. Those in the category *unsure* were then assigned to the other two categories by the other reviewer and additionally and independently by the leading investigator JP. Articles that were categorized as *relevant* by at least one reviewer were kept in the pool for full-text consultation.

5.2.1. *Selection criteria for articles based on title and/or abstract*

The following criteria for selecting articles from the search results were defined before the selection of relevant articles was started:

Inclusion criteria:

- Languages: English, German, Italian, French
- Publication type: original research manuscripts published in peer-reviewed journals, letters, editorials, meeting abstracts
- Study design: systematic reviews, meta-analyses, RCTs, case-control studies, case reports and studies and cohort studies
- Study population: human participants
- Case definition: Patient has a genetic diagnosis of a PID based on the international classification provided by the IUIS[17]
- Study outcomes: Death of at least one patient due to an infectious disease

Exclusion criteria:

- Publication type: narrative reviews, commentaries, unpublished manuscripts, dissertations, government reports, books and book chapters, conference proceedings, lectures and addresses, and consensus development statements (including guideline statements)
- Study design: cross-sectional studies, qualitative studies, non-systematic reviews, studies that did not report methods, and cadaveric, biomechanical, and laboratory studies
- Study population: animals
- Case definition: Patient without genetic PID diagnosis, patient still alive, patient with HIV infection. *(Later added: patient with cystic fibrosis)*

At this stage all types of study designs were included, but the ultimate aim has always been to identify individual cases and not the inclusion of synthesis or analysis results.

5.3. Data extraction and eligibility criteria on individual case level

Data was extracted from 32 articles in a test round to identify relevant data items. Using the results of this test round case level eligibility criteria were defined. A data extraction form with the following 7 items for each identified case was created:

1) *article reference*, 2) *additional article reference* with additional data cited by the first reference, 3) *patient identifier* in original text, 4) *gender*, 5) *gene*, 6) *mutation*, 7) *infectious agent(s)* that led to fatal outcome. An additional form was created for the patient history, allowing multiple chronological entries per identified case, using the following 5 fields: 1) *age*, 2) *patient data* including clinical history, clinical findings, family history, lab results etc., 3) *infectious agents* at that time, 4) received *treatment*, 5) reported *outcome*.

An 8th field was later added to each case record, to hold an assessment of the causal link between the mentioned infectious agent(s) and the cause of death as either *likely, possible* or *unlikely.*

Cases that matched the eligibility criteria were identified and only eligible articles were extracted by either MK or EK. For articles that did not yield any cases the reason for exclusion was noted.

5.3.1. *Eligibility criteria for data extraction*

The eligibility criteria have been refined during the early stages of data extraction. The final criteria are:

1) Death of the patient due to an infectious disease or a direct complication thereof (e.g. haemophagocytic lymphohistiocytosis).
2) A specific gene must be linked to the diagnosis of PID, preferably by mutation analysis if available at that time.
3) The infectious agent must be mentioned, not just the type of infection it caused.
4) The infectious agent(s) must be held at least partly responsible for the fatal outcome, i.e. a causal link must be suspected.
5) Therapeutic immunosuppression or transplantation is not a reason to exclude a case.
6) Outcomes and clinical features must be attributable to an individual patient, not just a cohort.

5.3.2. *Amendments to the eligibility criteria*

1) has been unchanged since the beginning of the process.
2) has been adapted to its current form to allow the inclusion of cases that have a clear gene association, but where mutational analysis has not been done. This concerns mostly cases that have been published a long time ago. Cases where the diagnosis was limited to a PID phenotype were not included, since the objective of this project is to aid in the choice of genes to test for known PID mutations.
3) has been added because an infection without reported infectious agent would not be specific enough to aid in decision making.
4) was added later to distinguish acute infections that patients died of, from chronic infections that patients died with, sometimes at old age.
5) was added as PID often has autoimmune or allergic components. Immunosuppression is also used before, during and after HSCT, yet patients still carry their inherent vulnerabilities with them up to a certain point. It remains difficult to distinguish the contributing factor of therapeutic immunosuppression from the inherent vulnerabilities in these cases.
6) was added because our data extraction form did not allow for the extraction of data that did not provide individual patient data.

5.4. Data management

A website was created for data entry into a relational database with editable table fields adapted to the above-mentioned data items, using SpryMedia DataTables and Editor software and custom scripts for sorting, filtering and rendering written in the JavaScript programming language. For consistency, all gene names were matched to the internationally recommended gene symbol, according to the HUGO Gene Nomenclature.[40] The names of infectious agents were matched to those found in the NCBI taxonomy database to ensure consistent naming.[41]

5.5. Quality assessment and evaluation for risk of bias

A random selection of 10 included selected cases was assessed on quality of reporting with the CARE guidelines[42], a checklist for the assessment of quality criteria in case reports. Since none of the selected studies mentioned the word case in their title this criterion is not listed in the results (Table 1). In its place the study type is mentioned. The random selection was performed with a random number generator in the Julia programming language version 1.0.0 with the following command: `rand(1:225, 10)`

For the quality assessment of case series a tool has recently been developed which is not used here however, since it is geared towards the assessment intervention effectiveness, which does not add any value for the type of question we are asking.[7,43]

5.6. Synthesis and analysis

A summary table was created, with the goal of making it easy to look up genetic diagnoses that occurred together with the various infectious agents that were mentioned in the fatal cases that were extracted. The table of extracted cases in Appendix G is sorted by gene as well, to facilitate this lookup process.

No further quantitative statistical analysis has been performed so far since we were not able to identify any meaningful analysis for the data. It is planned to consult with a statistics expert to discuss any suitable methods for the planned review.

5.7. Methodological self-evaluation

The PRISMA-P checklist was used to evaluate all important aspects that played a role in the setting up of this systematic review.[10]

5.8. Ethics

No ethics approval was required for this project, because all data used has previously been published.

6. Results

6.1. Search results

The article search was conducted on 5 February 2018. It resulted in a total of 3149 publications: 524 from EMBASE, 432 from MEDLINE, 157 from PUBMED and 2036 from SCOPUS. After automated deduplication, 2539 remained in the pool. Another 18 articles were added later to the pool if an included case cited a previous publication with further details on the same case. In total 2557 articles were screened for eligibility.

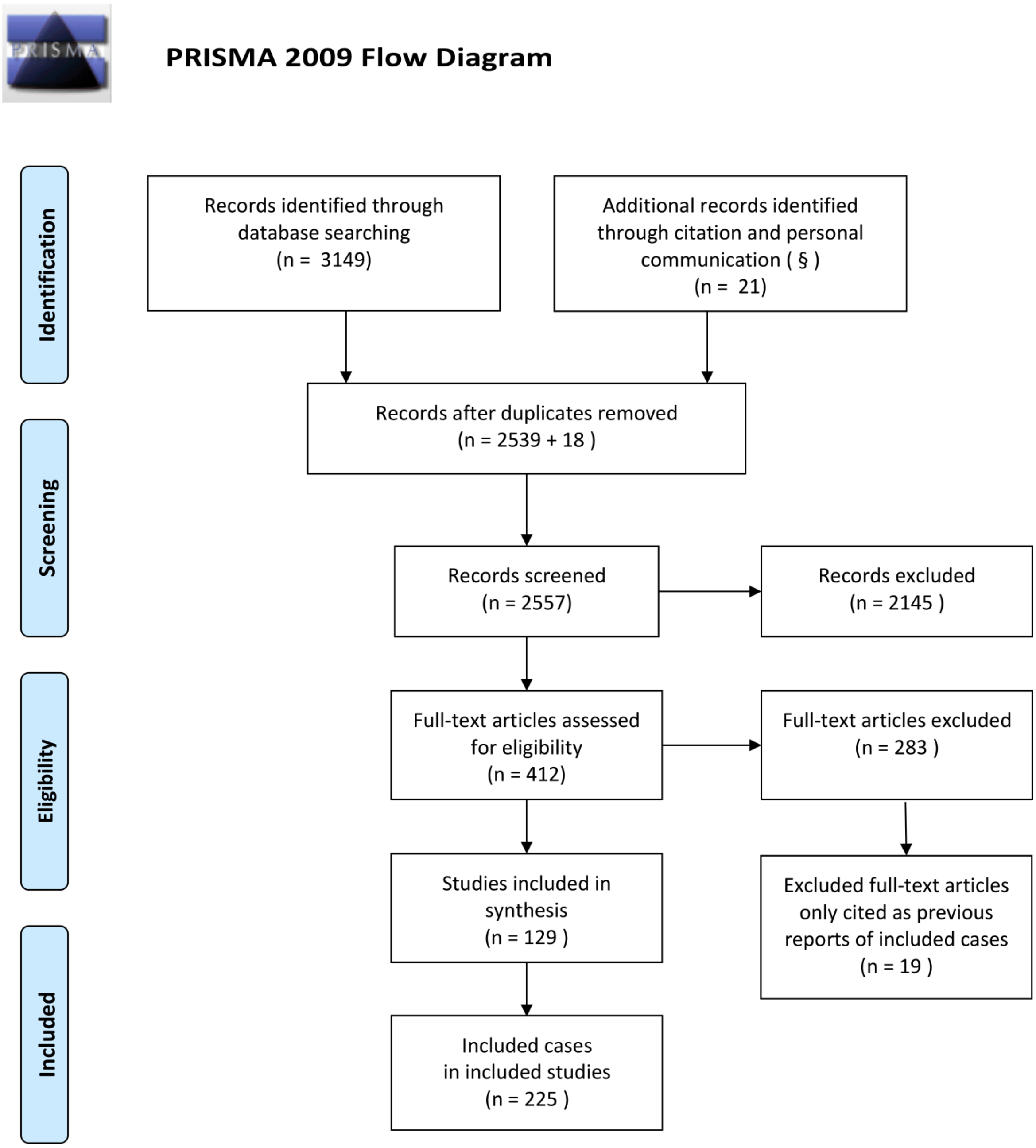


Figure 1: Prisma article selection flowchart

6.2. Selection of articles based on title and abstract

2074 articles were dismissed at first glance as off topic by at least 1 author. 191 articles were categorized as *unsure* and 70 thereof were independently dismissed by two authors in a second round. This left 394 articles from the original search query in the pool. Considering the additional 18 articles added at a later stage, a total of 412 articles were considered for full-text consultation and data extraction. See Appendix F for the full list of articles. Articles that have been added manually are marked in Appendix F with **§**.

6.3. Data extraction

Among the original 394 articles of which the full text was consulted, 267 articles did not yield any cases for various reasons: among them *no fatality mentioned*, *no infectious agent mentioned*, *case already included from another article* (data from both articles was then considered), *cause of death did not have a tangible link with any of the mentioned infections*, *no genetic diagnosis or clear gene candidate*, *no individual data available*. From the remaining 127 articles, 222 cases that met all eligibility criteria were extracted.

Of the included cases, 28 had referenced an article with additional data in one of 21 articles. These articles were added to the pool manually if they were not in it yet (which three of them were). The added 18 articles were also screened for eligible cases. Of those, two articles yielded another three new cases. Thus, the end result is 225 included cases in 129 articles. Of the 283 excluded articles, 19 still serve as additional data source for some included case, three from the original pool and 16 from the added articles. See Appendix G for extracted data from these 225 cases.

6.3.1. *Encountered problems*

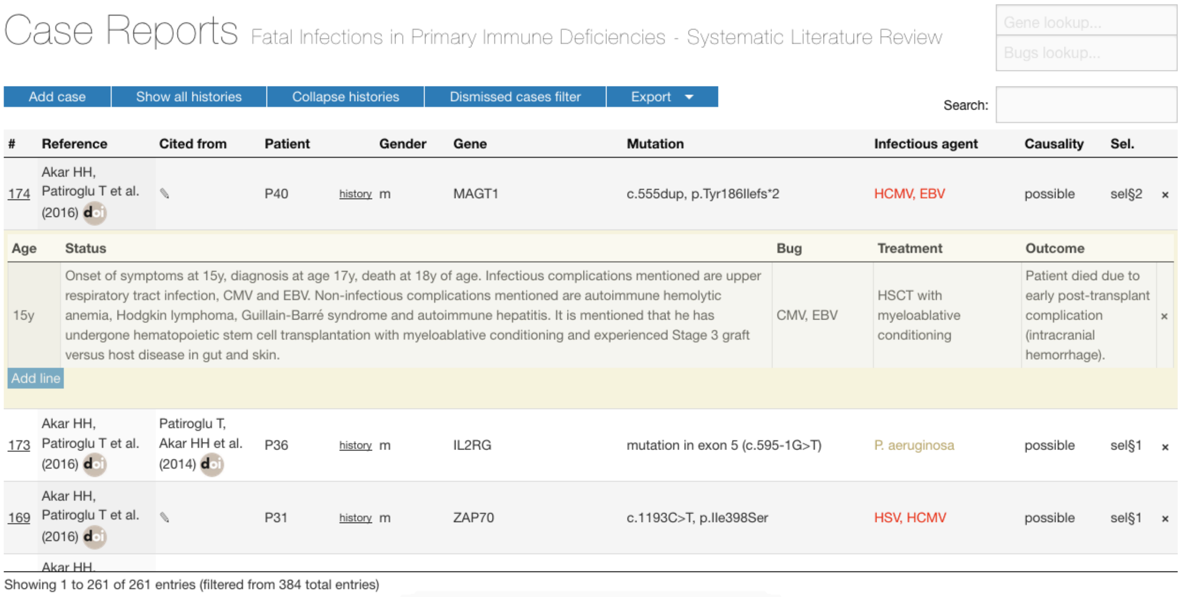
Among these 225 cases, there are 54, for which it remains unclear if there is a causal link between the mentioned infection and the cause of death. These cases are marked with the entry *possible* in appendix G. The causality was either difficult or impossible to evaluate in these cases, but none of them were completely implausible.

Another 15 cases only have a clinical diagnosis, but they seem to have a clear gene correlate. Two more cases have not undergone any mutational analysis, but their affected gene was implied by similar symptoms in family members that have a confirmed genetic diagnosis.

For another 36 extracted cases not included in the mentioned 225 cases, some issue has been identified, hindering inclusion, see Appendix H. Most of them have a questionable link between infection and fatality, making a causal link seemingly unlikely. Some of these may be included later if the cause of death can be clarified, for example by contacting the author.

6.4. Data management

The final interface of the data extraction website is represented below.



<u>Figure 2: Interface of data extraction website</u>

Note that the patient numbers in this figure do not correlate with the tables in this publication. P40 can be found in Appendix H as Q30, while P36 and P31 can be found in Appendix G as P120 and P223 respectivley.

The website in its current state is a prototype that has been developed especially for the purpose of this review. It is planned to develop this further into a generic tool that can be used by anyone working on a systematic review.

6.5. Quality assessment and evaluation for risk of bias

The quality of the timeline had the greatest impact on the quality of our results and had great variation. To our surprise, among the articles that performed worst for this criterion were also some case reports, while some cohort studies managed to provide this valuable data.

The results from the application of the CARE checklist to a random selection of 10 included articles is presented in Table 1. In our subjective perception, the overall quality of reporting in most articles was poor, while the evaluation of these 10 articles shows a rather modest proportion of articles with very poor reporting quality. Our perception is possibly thwarted, because those articles with the poorest reporting quality needed more attention to squeeze any useful data out of them, whereas those with adequate reporting took little effort to extract.

Apart from the missing timeline, minimal or no data on the cause of death and the nature of the infection, many reports did not manage to report which therapeutic interventions the patients had undergone and most of the time no mention was made of the efficacy of those interventions. The timeline is essential to evaluate the causal link between an infectious event and a fatal outcome.

Table 1: CARE assessment of 10 included articles

<table>
<tr><th>Assessment criteria</th><th>Alkhairy (14)</th><th>Avila (19)</th><th>Beaussant (39)</th><th>Cannioto (60)</th><th>Del Giudice (87)</th><th>Grace (129)</th><th>Mancebo (233)</th><th>Okuno (275)</th><th>Orange (277)</th><th>Szczawinska (369)</th></tr>
<tr><td>Study design</td><td>case study</td><td>case series</td><td>prospective cohort</td><td>retrospective cohort</td><td>case study</td><td>case study</td><td>case study</td><td>case study</td><td>case series</td><td>case report</td></tr>
<tr><td>Keywords</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>missing</td><td>adequate</td><td>adequate</td><td>adequate</td><td>missing</td></tr>
<tr><td>Abstract</td><td>minimal</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td></tr>
<tr><td>Introduction</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>missing</td></tr>
<tr><td>Patient information</td><td>adequate</td><td>adequate</td><td>adequate</td><td>limited</td><td>adequate</td><td>adequate</td><td rowspan="7">the main case is described adequately, the cited case only minimally, but the latter is described adequately in its original publication.</td><td>adequate</td><td>adequate</td><td>adequate</td></tr>
<tr><td>Clinical findings</td><td>adequate</td><td>adequate</td><td>adequate</td><td>minimal</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td></tr>
<tr><td>Timeline</td><td>adequate</td><td>adequate</td><td>adequate</td><td>missing</td><td>excellent</td><td>excellent</td><td>adequate</td><td>recon-structable</td><td>missing</td></tr>
<tr><td>Diagnostic assessment</td><td>adequate</td><td>adequate</td><td>adequate</td><td>missing</td><td>excellent</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td></tr>
<tr><td>Therapeutic intervention</td><td>adequate</td><td>minimal</td><td>adequate</td><td>minimal</td><td>excellent</td><td>adequate</td><td>adequate</td><td>minimal</td><td>minimal</td></tr>
<tr><td>Follow-up & Outcomes</td><td>adequate</td><td>minimal</td><td>adequate</td><td>minimal</td><td>excellent</td><td>adequate</td><td>adequate</td><td>minimal</td><td>minimal</td></tr>
<tr><td>Discussion</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td><td>adequate</td></tr>
<tr><td>Patient Perspective</td><td>missing</td><td>missing</td><td>missing</td><td>missing</td><td>missing</td><td>missing</td><td>missing</td><td>missing</td><td>missing</td><td>missing</td></tr>
<tr><td>Informed Consent</td><td>missing</td><td>adequate</td><td>adequate</td><td>missing</td><td>missing</td><td>missing</td><td>ethics committee approval</td><td>provided for gene sequencing</td><td>adequate</td><td>missing</td></tr>
</table>

adequate = essential data provided in concise format, minimal = only some data provided, excellent = above average, missing = no interpretation possible due to missing data.

6.6. Synthesis of collected data on fatal infections in PID

The synthesis tables are divided into one summary table (Table 2) and four tables with various categories of infectious agents in more detail:
viruses (Table 3), gram-negative bacteria (Table 4), other bacteria (Table 5) and finally fungi and protozoans (Table 6). Since several pathogens may be involved in a single case, such cases are represented multiple times, accounting for in total 375 relevant occurrences of an infectious agent in 225 fatal cases (see appendix G for details).

For each combination of infectious agent and gene, the total number of cases where this combination occurred is given. The total number of occurrences and the total number of unique genes associated with is calculated for each mentioned pathogen, as well as for several levels in the taxonomy, such as Klebsiella (all species), gram-negative bacteria, all bacteria, etc. For each gene, the number of cases is given, as wells as the number of distinct pathogens found.

The total number of unique PID related genes was 64, but two of those occurred only once and in the same case. A third mutation in that same case of the gene XKR3 is not known to cause PID. This combination of three genes was included as one entity in the table. The total number of distinct entities of infectious agents as mentioned in the original articles was 87, of which 25 viruses, 44 entities of bacteria, from rather unspecific (gram-positive bacteria) to very specific (N. meningitides serotype C), 13 entities of fungi (of which most were either some species of Aspergillus or Candida) and 5 entities of protozoans.

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	Number of cases	Distinct pathogens	Any Pathogen	Any Virus	Any Bacteria	Any Fungi	Any protozoan
ADA	6	6	7	5		2	
*ADA2, IL17R and XKR3**	1	2	2		1	2	
ADAM17	2	2	2	2			
AP3B1	1	2	2	2			
ATM	1	1	1	1			
BTK	6	5	10	2	8		
C1QB	1	1	1			1	
C2	4	2	5		5		
C3	1	1	1		1		
CARD11	2	7	10	4	6		
CARD9	5	3	5			5	
CD27	5	5	8	5	1	1	1
CD40	2	2	2		1		1
CD40LG	13	14	21	2	8	4	7
CD8A	1	1	1		1		
CFP	3	2	3		3		
CXCR4	2	4	4	2	2		
CYBB	4	7	7		6	1	
DCLRE1C	6	4	6	2		2	2
DKC1	1	1	1		1		
DNMT3B	3	4	5	1	3	1	
DOCK2	2	6	6	4	2		
DOCK8	6	10	20	12	1	4	3
FAAP24	2	1	2	2			
FOXP3	7	7	13		12	1	
GATA2	7	11	17	10	5	2	
ICOS	1	4	4	3			1
IFNGR1	1	1	1		1		
IFNGR2	3	1	2		2		
IKBKB	1	4	4	1	3		
IKBKG	14	18	29	1	21	7	
IL12B	2	3	3		3		
IL12RB1	3	2	4		3	1	
IL2RG	9	7	11	4	6	1	
IRAK4	5	2	5		5		
ITGB2	1	3	3		3		
ITK	2	1	2	2			
LRBA	1	4	4		3	1	
LYST	1	1	1	1			
MAGT1	2	2	3	1	2		
NCF2	2	2	3		1	2	
NFKBIA	5	9	11		8	3	
PGM3	1	1	2		2		
PIK3R1	1	3	3		3		
PNP	3	4	4	1	2	1	
PRF1	4	3	5	4	1		
RAB27A	1	1	1	1			
RAC2	1	1	1		1		
RAG1	11	12	14	4	7	3	
RAG2	6	9	11	6	3	1	1
RMRP	1	3	3		3		
RTEL1	1	1	1	1			
SH2D1A	9	2	10	9		1	
STAT1	4	4	4	4			
STAT3	3	2	3		2	1	
TRNT1	1	1	2		2		
TTC37	3	6	7	2	5		
UNC13D	1	1	1	1			
WAS	22	18	45	17	24	4	
WDR1	1	1	1	1			
XIAP	1	1	1	1			
ZAP70	1	2	2	2			
ZBTB24	2	2	2		1	1	
Total occurrences			**375**	**123**	**184**	**52**	**16**

Table 2: Overview of pathogen types for each PID

The numbers represent the number of times a pathogen in that category was believed to play a role in a fatal outcome. More than one pathogen was mentioned in several cases and then each pathogen was counted as an occurrence, accounting for 375 occurrences in 225 cases. The number of distinct pathogens is given for all cases of the same gene, as well as the number of cases per gene.

* XKR3 mutations are not known to cause PID. ADA2 was previously known as CECR1.

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Table 3: PIDs with reported fatal viral infection

Gene	Cases per gene, total n = 225 cases	Distinct pathogens per gene	All pathogens, total	Virus, total	Bacteria, total	Fungi, total	Protozoan, total	Coxsackievirus (CoxV)	Epstein-Barr virus (EBV)	Hepatitis B virus (HBV)	Hepatitis C virus (HCV)	Herpes simplex virus (HSV)	Human adenovirus (HAdV)	Human herpesvirus 6 (HHV6)	Human cytomegalovirus (HCMV)	Human papillomavirus (HPV)	Human parvovirus B19 (PVB19)	Human RSV (HRSV)	Influenza A H1N1 (H1N1)	Influenza B virus (FLUBV)	J.C. polyomavirus (JCPyV)	Jamestown canyon virus (JaCaV)	Metapneumovirus	Mumps Jeryll Lynn, vaccine	Norovirus (NoV)	Parainfluenza virus III (HPIV-3)	Parainfluenza virus, unspecific	Rhinovirus	Rotavirus	Rubella RA27/3, vaccine	Varicella zoster virus (VZV)	VZV Oka, vaccine
ADA	6	6	7	5		2									2						1					1	1					
ADAM17	2	2	2	2													1	1														
AP3B1	1	2	2	2					1						1																	
ATM	1	1	1	1					1																							
BTK	6	5	10	2	8					1				1																		
CARD11	2	7	10	4	6										2								1					1				
CD27	5	5	8	5	1	1	1	1	4																							
CD40LG	13	14	21	2	8	4	7	1							1																	
CXCR4	2	4	4	2	2										1	1																
DCLRE1C	6	4	6	2		2	2		2																							
DNMT3B	3	4	5	1	3	1																									1	
DOCK2	2	6	6	4	2								1		1											1					1	
DOCK8	6	10	20	12	1	4	3		5	1	1	1			4																	
FAAP24	2	1	2	2					2																							
GATA2	7	11	17	10	5	2			1		1	3			1	3															1	
ICOS	1	4	4	3			1						1	1											1							
IKBKB	1	4	4	1	3							1																				
IKBKG	14	18	29	1	21	7							1																			
IL2RG	9	7	11	4	6	1			1						3																	
ITK	2	1	2	2					2																							
LYST	1	1	1	1															1													
MAGT1	2	2	3	1	2				1																							
PNP	3	4	4	1	2	1									1																	
PRF1	4	3	5	4	1				3														1									
RAB27A	1	1	1	1					1																							
RAG1	11	12	14	4	7	3									2						1				1							
RAG2	6	9	11	6	3	1	1								2									1		1				1		1
RTEL1	1	1	1	1																											1	
SH2D1A	9	2	10	9		1			9																							
STAT1	4	4	4	4					1						1						1	1										
TTC37	3	6	7	2	5										1			1														
UNC13D	1	1	1	1																									1			
WAS	22	18	45	17	24	4			5		1	1			6					1	1										2	
WDR1	1	1	1	1																											1	
XIAP	1	1	1	1					1																							
ZAP70	1	2	2	2								1			1																	
total occurrences			375	123	184	52	16	2	40	2	3	7	3	2	30	4	1	2	1	1	4	1	2	1	2	3	1	1	1	1	7	1
distinct PIDs			63	36	44	25	7	2	16	2	3	5	3	2	16	2	1	2	1	1	4	1	2	1	2	3	1	1	1	1	6	1

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Table 4: PIDs with reported fatal gram-negative bacterial infection

	distinct PIDs	total occurrences	ZBTB24	WAS	TTC37	RMRP	RAG2	RAG1	PRF1	PNP	PIK3R1	NFKBIA	LRBA	ITGB2	IRAK4	IL2RG	IL12B	IKBKG	IKBKB	FOXP3	DOCK2	DNMT3B	DKC1	CYBB	CXCR4	CFP	CD8A	CD40LG	CD40	CARD11	BTK	ADA2, IL17RA, XKR3
Cases per gene, total n = 225 cases			2	22	3	1	6	11	4	3	1	5	1	1	5	9	2	14	1	7	2	3	1	4	2	3	1	13	2	2	6	1
Distinct pathogens per gene			2	18	6	3	9	12	3	4	3	9	4	3	2	7	3	18	4	7	6	4	1	7	4	2	1	14	2	7	5	2
All pathogens, total	63	375	2	45	7	3	11	14	5	4	3	11	4	3	5	11	3	29	4	13	6	5	1	7	4	3	1	21	2	10	10	2
Virus, total	36	123		17	2		6	4	4	1						4		1	1		4	1			2			2		4	2	
Bacteria, total	44	184	1	24	5	3	3	7	1	2	3	8	3	3	5	6	3	21	3	12	2	3	1	6	2	3	1	8	1	6	8	1
Fungi, total	25	52	1	4			1	3		1		3	1			1		7		1		1		1				4				1
Protozoan, total	7	16					1																					7	1			
Gram (-) bacteria, (GNB), total	30	76	1	4	2	1	1	3	1	1	2	5	2	2	1	3	1	7	2	8	1	3	1	4	1	3	1	7	1	2	4	1
GNB (not further specified)	2	2						1				1																				
Acinetobacter, total	4	4										1	1											1				1				
Acinetobacter (not specified)	2	2											1															1				
A. baumannii	1	1																						1								
A. lwoffii	1	1										1																				
Aeromonas	1	1		1																												
B. cepacia	1	1																						1								
C. indologenes	1	1						1																								
C. jejuni	1	1									1																					
E. cloacae	1	1					1																									
E. coli	3	4																2					1					1				
Enterobacter	2	2																	1	1												
H. influenzae	2	2				1												1														
Klebsiella, total	10	15			2					1		1		1				1		4	1	2						1		1		
Klebsiella, not specified	4	6			1															2		2								1		
K. oxytoca	1	1																1														
K. pneumoniae	7	8			1					1		1		1						2	1							1				
N. meningitidis	1	2																								2						
N. meningitidis C	1	1																								1						
Nocardia	1	1		1																												
P. aeruginosa	16	27	1	1					1			1			1	2		3		3		1			1		1	4	1	1	4	1
S. maltophilia	4	4										1		1					1					1								
S. marcescens	1	1											1																			
Salmonella, total	6	6		1				1			1					1	1							1								
Salmonella, not specified	2	2														1								1								
Sal. ser. Enteritidis	1	1						1																								
Sal. ser. Typhimurium	1	1									1																					
Salmonella B	2	2		1													1															
Gram (+) bacteria (GPB), total	23	74		20	3	1		2			1	3	1	1	4	2		7		4								1		4	4	
Acid-fast bacteria, total	17	34				1	2	2		1						1	2	7	1		1			2	1							

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Table 5: PIDs with reported fatal gram-positive or acid-fast bacterial infection

	distinct PIDs	total occurrences	WAS	TTC37	TRNT1	STAT3	RMRP	RAG2	RAG1	RAC2	PNP	PIK3R1	PGM3	NFKBIA	NCF2	MAGT1	LRBA	ITGB2	IRAK4	IL2RG	IL12RB1	IL12B	IKBKG	IKBKB	IFNGR2	IFNGR1	GATA2	FOXP3	DOCK8	DOCK2	CYBB	CXCR4	CD40LG	CD27	CARD11	C3	C2	BTK
Cases per gene, total n = 225 cases			22	3	1	3	1	6	11	1	3	1	1	5	2	2	1	1	5	9	3	2	14	1	3	1	7	7	6	2	4	2	13	5	2	1	4	6
Distinct pathogens per gene			18	6	1	2	3	9	12	1	4	3	1	9	2	2	4	3	2	7	2	3	18	4	1	1	11	7	10	6	7	4	14	5	7	1	2	5
All pathogens, total	63	375	45	7	2	3	3	11	14	1	4	3	2	11	3	3	4	3	5	11	4	3	29	4	2	1	17	13	20	6	7	4	21	8	10	1	5	10
Virus, total	36	123	17	2				6	4		1					1				4			1	1			10		12	4		2	2	5	4			2
Bacteria, total	44	184	24	5	2	2	3	3	7	1	2	3	2	8	1	2	3	3	5	6	3	3	21	3	2	1	5	12	1	2	6	2	8	1	6	1	5	8
Fungi, total	25	52	4			1		1	3		1			3	2		1			1	1		7				2	1	4		1		4	1				
Protozoan, total	7	16						1																					3				7	1				
Gram (-) bacteria, (GNB), total	30	76	4	2			1	1	3		1	2		5			2	2	1	3		1	7	2				8		1	4	1	7		2			4
Gram (+) bacteria (GPB), total	23	74	20	3	2	2	1		2	1		1	2	3		2	1	1	4	2			7					4					1	1	4	1	5	4
GPB, not further specified	1	1																																1				
C. difficile	1	1										1																										
Enterococcus	4	5		1													1						1												2			
E. faecium	3	3												1				1					1															
L. monocytogenes	1	1																					1															
Staphylococcus, total	13	21	8	1	1				1				1	1		1				1			1					2							1		1	1
Coagulase-negative species	3	3							1											1								1										
Methicillin-resistant S. aureus (MRSA)	1	1	1																																			
S. aureus	11	17	7	1	1								1	1		1							1					1							1		1	1
Streptococcus, total	10	21	4			2	1			1									4				2										1			1	3	2
S. agalactiae	1	1	1																																			
S. pneumoniae	9	18	3			2	1												4				1										1			1	3	2
S. pyogenes	1	1								1																												
S. viridans	1	1																					1															
Acid-fast bacteria, total	17	34					1	2	2		1				1					1	3	2	7	1	2	1	5		1	1	2	1						
Bacille Calmette-Guérin (BCG)	8	12						2	1											1	3	1			2					1	1							
Mycobacterium, not specified	2	2																					1									1						
M. bovis	1	1																						1														
M. catarrhalis	2	2					1																						1									
M. chelonae	2	2																				1					1											
M. kansasii	1	2																									2											
M. avium complex (MAC)	4	10							1														6			1	2											
M. tuberculosis (TB)	3	3									1				1																1							

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Table 6: PIDs with reported fatal fungal or protozoan infection

	Cases per gene, total n = 225 cases	Distinct pathogens per gene	All pathogens, total	Virus, total	Bacteria, total	Fungi, total	Protozoan, total	Fungi, not further specified	Aspergillus, total	*Aspergillus, not specified*	*A. flavus*	*A. fumigatus*	Blastomyces	Candida, total	*Candida (not further specified)*	*C. glabrata*	*C. krusei*	*C. lusitaniae*	*C. parapsilosis*	Cryptococcus	P. carinii	P. jirovecii	T. violaceum	Cryptosporidium, total	*Cryptosporidium (not further specified)*	*C. parvum*	G. lamblia	I. belli	T. gondii
ADA	6	6	7	5		2		1						1	1														
ADA2, IL17RA, XKR3	1	2	2		1	1								1	1														
C1QB	1	1	1			1															1								
CARD9	5	3	5			5		1	1			1											3						
CD27	5	5	8	5	1	1	1							1	1														1
CD40	2	2	2		1		1																	1	1				
CD40LG	13	14	21	2	8	4	7		1	1				2	2					1				2		2	1	1	3
CYBB	4	7	7		6	1			1	1																			
DCLRE1C	6	4	6	2		2	2		2	2														1	1				1
DNMT3B	3	4	5	1	3	1																1							
DOCK8	6	10	20	12	1	4	3	1	1		1			2	2									3	3				
FOXP3	7	7	13		12	1															1								
GATA2	7	11	17	10	5	2							1	1	1														
ICOS	1	4	4	3			1																	1	1				
IKBKG	14	18	29	1	21	7			1			1		4	2	1		1			2								
IL12RB1	3	2	4		3	1								1	1														
IL2RG	9	7	11	4	6	1			1	1																			
LRBA	1	4	4		3	1								1			1												
NCF2	2	2	3		1	2			2	2																			
NFKBIA	5	9	11		8	3								3	2				1										
PNP	3	4	4	1	2	1			1			1																	
RAG1	11	12	14	4	7	3			1	1				1	1							1							
RAG2	6	9	11	6	3	1	1		1	1																	1		
SH2D1A	9	2	10	9		1			1	1																			
STAT3	3	2	3		2	1																1							
WAS	22	18	45	17	24	4			1	1				2	2						1								
ZBTB24	2	2	2		1	1																1							
total occurrences			375	123	184	52	16	3	15	11	1	3	1	20	16	1	1	1	1	1	5	4	3	8	6	2	2	1	5
distinct PIDs			63	36	44	25	7	3	13	9	1	3	1	12	11	1	1	1	1	1	4	4	1	5	4	1	2	1	3

6.7. Methodological self-evaluation

Table 7: PRISMA-P 2015 checklist applied to this review process

Section/topic	Item #	Result of self-evaluation
ADMINISTRATIVE INFORMATION		
Title		
Identification	1a	The publication will have the term *systematic review* in the title.
Update	1b	The first protocol is in the process of submission.
Registration	2	A protocol has been submitted to PROSPERO but not published so far.
Authors		
Contact	3a	An email address is available in chapter *9: Authors' contributions*.
Contributions	3b	Chapter *9: Authors' contributions* elaborates on the contributions of each author.
Amendments	4	Amendments are mentioned in chapter *5: Methods*.
Support		
Sources	5a	Expenses for obtaining full-text articles were paid by the Pachlopnik research lab.
Sponsor	5b	No sponsor was involved in this project.
INTRODUCTION		
Rationale	6	The rationale is explained in chapter *4.3: Infections in PID.*
Objectives	7	The objective of this review is mentioned in chapter *4.4: Objective.*
METHODS		
Eligibility criteria	8	The eligibility criteria are presented in chapters *5.2.1* and *5.3.1*.
Information sources	9	All information sources are declared in chapter *5.1: Search strategy and data sources.*
Search strategy	10	The general search strategy is presented in chapter *5.1.1.*
Study records		
Data management	11a	The software used is briefly mentioned in chapter *5: Methods*.
Selection process	11b	The selection process is described in chapters *5.2* and *5.3.*
Data collection process	11c	The data collection process is mentioned in chapter *5.3*.
Data items	12	The data items sought are all mentioned in chapter *5.3.*
Outcomes and prioritization	13	The outcomes sought are mentioned in chapter *4.4: Objectives.*
Risk of bias in individual studies	14	Reporting quality and is analyzed for a random sample in chapter *6.5: Quality assessment and evaluation for risk of bias.*
Data synthesis		
Criteria	15a	No criteria for quantitative analysis have been developed yet.
Planned methods	15b	A descriptive analysis is planned.
Additional analyses	15c	To be evaluated after consultation with statistics expert.
Alternative synthesis	15d	To be evaluated after consultation with statistics expert.
Meta-bias	16	Bias is addressed in chapter *7.4: Introduction of new bias*
Confidence in cumulative evidence	17	See chapter *7.6: Conclusion.*

7. Discussion

7.1. Most important results

This interim evaluation of extracted data reveals that of more than 300 possible genetic diagnoses of PID, this review managed to identify 64 mutated PID genes with at least one fatal case at least in part attributable to infection. A large number of distinct pathogens was identified, among them approximately 25 distinct species of viruses, ~44 distinct species of bacteria, ~13 species of fungi (mostly some species of Aspergillus or Candida) and ~5 species of protozoans.

The presented tables allow quick lookup of previously reported combinations of PID and specific pathogens in the medical literature. Many case reports could be found as part of study designs other than classical case reports.

Setting up a systematic review needs careful preparation and take into account various challenges, among them: how to deal with interobserver variability, how to deal with low quality of reporting and how to manage organize extracted data in a meaningful way.

7.2. Comparison to other publications

A simple search on PUBMED with the search terms “systematic review” and “PID” identified 11 systematic reviews related to primary immunodeficiency with various focuses. The diagnostic utility of new generation sequencing was reviewed[44], whereas in the category of interventions, two reviews looked at subcutaneous immunoglobulin therapy[45], one of them focusing on patient preference compared to intravenous immunoglobulin.[46] One review with a psychometric focus looked at the quality of life of patients living with PID.[47] Epidemiological data was analysed in a review looking at the prevalence of consanguinity in the PID population compared to a healthy population[48], a review that looked at the prevalence of lymphoma in the PID population[49] and another review focused on the prevalence of malignancy in CVID[50]. One review looked at the various categories of PIDs in children and highlights their association with various malignancies, but even though it claims to be a systematic review in the title, no methods are described and the content of the article is remarkably short fur such an extensive field of interest, which makes it questionable how systematic it can be considered.[51] Similarly, another review looked specifically at the mechanisms involved in EBV-induced lymphoproliferative disorder and gives extensive descriptions of the mechanisms described in various literature, but methods are not mentioned.[52] The physiopathology of vaccine-derived poliovirus infection in patients with PID was reviewed systematically last year.[53] Most pertinent to the topic of this thesis is the review done on the prevalence of PID in children with invasive pneumococcal infection in the absence of predisposing conditions.[24]

The most important difference of the latter to our review is that it takes the prevalence of PID within a specific population (invasive infection) into account, which is not possible to derive from a series of case reports focusing on PID.

7.3. Strengths and limitations

The work on this project has allowed the author to gain familiarity with the tools and checklists used for systematic reviews and to develop a prototype for a data management tool that may ultimately be useful for any researcher working on a systematic review. Valuable experience in the conduction of a systematic review has been gathered, which now allows for the careful planning and conduction of a systematic review on the infectious causes of death in specific PIDs.

Critical reflection on this work has led to increased confidence in the utility of the results: the author is confident that the generated results provide useful suggestions of genetic candidates to screen for, when managing patients with life-threatening infections. These suggestions are based on the assumption that events in the future will resemble observations that have been made in the past in similar circumstances. This principle is known as inductive inference, on which empirical evidence is based.[54] It is common in medicine and other professions to use the best available explanation for an observation to guide future actions.[55] Of course, testing the validity and assessing the predictive value of the proposed associations between specific pathogens and specific PIDs will further increase confidence in those associations that hold up to scientific scrutiny, while some other associations will prove to be mere noise in the sampled data.[55]

Looking closely at the used method has also led to the exploration of methodological considerations of systematic reviews and this has led to the exposure to evolved study designs such as the "systematic *mapping* review". These have the property that the focus is more on making all available knowledge that may help in answering a question accessible in a structured way (mapping) and less on authoritatively answering a question, except for the basic question: "What do we know so far?".[56,57,58]
It is also used as a tool to identify knowledge gaps and areas in need of further research.[59]
A large number of publications was summarized in this work and the resulting table of occurrences of fatal infections in several PIDs allows for fast access to a large comprehensive body of data on fatal infections in PID.

Some limitations are apparent in this work. Firstly, the validity of the results is limited by publication bias. Somewhat related, a large number of otherwise eligible studies had to be excluded from this review because the authors failed to mention the pathogens that were responsible for the infectious event, so even if a case of fatal infection in PID is published, it doesn't necessarily provide all the needed details for a synthesis of outcomes.

Secondly, the assessment of causality and the reconstruction of a chain of events leading to death based on incomplete data is prone to error, including interobserver variability, limiting the reproducibility of this work.

Furthermore, the significance of an occurrence of a fatal infection is difficult to judge without the epidemiological context of such events. Some pathogens are deadly for any human being and the difference would not the occurrence itself, but the increased incidence of such events in a vulnerable population. This is less of a problem for opportunistic pathogens, which generally do not cause disease in immunocompetent individuals. Unfortunately, a comparison of incidence and mortality rates for pathogenic infections between PID and general populations is nearly impossible, due to the lack of such data. Taking into account the general pathogenicity and mortality rate in the general population of identified pathogens may be simplified by pointing to sources of such data.

From a methodological perspective, two issues need attention. Firstly, the focus of this review was limited to the synthesis of the outcome of individual cases. Previously synthesized data that answers the same question was not taken into account. To adjust for this, it may be possible to adapt the search strategy to include other terminology such as *susceptibility*, *incidence* and other keywords that would need to be explored.

Secondly, the final selection of articles was assessed for eligibility of data extraction by two researchers (MK and KE), each one dealing with approximately 210 articles. A large portion of studies was thus assessed by just one researcher. During the preparation of this manuscript the reasons for exclusion in Appendix F were unified, because these were written in free-text and partly in German. During this process, it seemed that both researchers have failed to include a considerable amount of eligible cases. The results as described in Chapter 6, do not yet take this observation into account and a second round of data extraction will be needed before the publication of this work. This shows how important a second look is for the reliability of data extraction, as is recommended in the guidelines.[9]

Regardless of all its limitations the gathered data is useful even now for the clinician that has to decide where to search for mutations, if considered in the context of its limiting factors. The future may tell if the suggestions provided here have a predictive value.

7.4. Introduction of new bias

Two major sources of bias were identified in this work:

Firstly, the difficulty in judging the cause of death from incomplete case reports. Extracting an outcome that is mentioned only on a side note is necessarily prone to the pitfalls of inductive reasoning. Especially if the timeline is missing from the patient history. On the other hand, even if all case reports would go to great lengths to discuss the chain of events leading to death, it would still be impossible to know if the pathogenicity of the infectious agent or the susceptibility of the patient contributed more to the fatal outcome. This limitation is partly also due to in the nature of a case report. Not excluding cases with therapeutic immunosuppression and post-HSCT add another confounding factor to this issue. Some outcomes that we report as fatal infection in PID will therefore be attributable to causes other than PID.

Secondly, many identified cases of fatal infection in PID will not be reported in academic literature. Only if an author deems a case of special interest, will the effort be taken to write a report for the academic community. The results presented here thus need to be viewed as a sub-set of possible outcomes. This problem would present in any retrospective study design. In our case the selection of patients was made by the authors of the case reports. To avoid this publication bias, a data source with prospective patient selection may be used, such as a patient registry.

7.5. Significance and implications for practice

A clinician that is faced with a severely ill child with high suspicion for untypical infection may wonder where to start in an attempt at diagnosing PID. It's like looking for a needle in a haystack, there are just so many avenues to explore. This work attempts to provide a suggestion on possible starting points, based on the assumption that what has been may repeat itself in the future. The bright side about PID is that a working therapy exists. The biggest challenge is in identifying those patients that may benefit from it.[60]

Presenting with severe infection is the best hint we may get that a patient could have PID. Taking into account which PIDs have struggled with the same pathogen in similar cases may be a helpful approach in making our guesses slightly more accurate.

7.6. Conclusion

Data extraction is a process prone to human error. All data extraction therefore needs to be done independently by at least two authors and findings need to be discussed and compared in peer group meetings. This helps to identify and eliminate such errors.

Systematic mapping review should be considered as a possible alternative methodology. This would imply the shift of focus away from distilling all available evidence into a recommendation towards presenting all available knowledge in a way that allows for efficient identification of relevant data that may be relevant for clinical decision making.

PID registries should be evaluated as possible data sources for validating the results in this review. Available epidemiological data on the identified pathogens should be pointed to, to put our results in context.

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9. Authors' contributions

JP Leading investigator: Prof. Dr. med. Dr. phil. nat. Jana Pachlopnik Schmid

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The original concept of this research project was developed by JP, together with AM. They also developed the general search strategy and the original selection criteria. MK and KE tried to apply these selection criteria to a subset of articles and compared the results with each other, with a suggestion leading to a minor change to the original selection criteria. A proposal for a data extraction table was then made by JP. Changes to this table were suggested by MK and KE and discussed in a group meeting, which led to the final version.

Selecting articles by title and/or abstract was done for slightly more than half of all articles each by KE and MK. Some overlap allowed the comparison of results for inconsistencies. The articles categorized as *not sure* were sorted by the other co-author and independently by JP. The final selection was evaluated by MK (including any article that was deemed relevant by any author).

The full-text pdfs were sourced by MK, with some help from the library for difficult to access articles. The website for data extraction was developed by MK. Half the articles were extracted by KE and half by MK. AM and JP were consulted several times when uncertainties emerged on how to proceed.

The manuscript of this thesis was written entirely by MK, with proofreading and editorial suggestions provided by KE and editorial suggestions by JP and AM. The tables and figures in this manuscript were created by MK alone.

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Last but not least, I would like to thank the patients and their families for sharing their data with the scientific community, for the purpose of furthering knowledge which will hopefully lead to more effective and less dangerous cures in the future.

11. Appendices

11.1. Appendix A – Search terms used for EMBASE

#1: 93065 results
((fatal:ti,ab OR death:ti,ab OR lethal:ti,ab OR deadly:ti,ab OR severe:ti,ab OR recurrent:ti,ab OR died:ti,ab OR succumbed:ti,ab OR deceased:ti,ab OR expired:ti,ab OR 'passed away':ti,ab OR perished:ti,ab) AND (infection*:ti,ab OR infected:ti,ab OR 'infectious disease*':ti,ab OR inflammat*:ti,ab OR seps*:ti,ab OR septic:ti,ab OR bacteremia*:ti,ab OR abscess*:ti,ab OR 'pulmonary infection*':ti,ab OR pneumonia:ti,ab OR mastoidit*:ti,ab OR sinusit*:ti,ab OR otit*:ti,ab OR epiglottit*:ti,ab OR meningit*:ti,ab OR encephalit*:ti,ab OR endocardit*:ti,ab OR 'catheter-related':ti,ab OR 'line-related':ti,ab OR 'chronic diarreha*':ti,ab OR peritonit*:ti,ab OR cholecystit*:ti,ab OR cholangit*:ti,ab OR 'urinary tract infection*':ti,ab OR cellulit*:ti,ab OR 'necrotising fasciit*':ti,ab OR 'necrotizing fasciit*':ti,ab OR myonecros*:ti,ab OR impetigo:ti,ab OR folliculit*:ti,ab OR osteomylit*:ti,ab) OR 'infection'/exp OR 'inflammation'/exp OR 'respiratory failure'/exp OR 'respiratory failure':ti,ab) AND ('fatality'/exp OR 'cause of death'/exp OR 'autopsy'/exp)

#2: 522451 results
il2rg:ti,ab OR jak3:ti,ab OR il7r:ti,ab OR ptprc:ti,ab OR cd3d:ti,ab OR cd3e:ti,ab OR cd247:ti,ab OR coro1a:ti,ab OR lat:ti,ab OR rag1:ti,ab OR rag2:ti,ab OR dclre1c:ti,ab OR prkdc:ti,ab OR nhej1:ti,ab OR lig4:ti,ab OR ak2:ti,ab OR ada:ti,ab OR dock2:ti,ab OR cd40lg:ti,ab OR tnfsf5:ti,ab OR cd40:ti,ab OR tnfrsf5:ti,ab OR icos:ti,ab OR cd3g:ti,ab OR cd8a:ti,ab OR tap1:ti,ab OR tap2:ti,ab OR tapbp:ti,ab OR b2m:ti,ab OR ciita:ti,ab OR rfxank:ti,ab OR rfx5:ti,ab OR rfxap:ti,ab OR dock8:ti,ab OR rhoh:ti,ab OR stk4:ti,ab OR trac:ti,ab OR lck:ti,ab OR malt1:ti,ab OR bcl10:ti,ab OR bcl11b:ti,ab OR il21:ti,ab OR il21r:ti,ab OR tnfrsf4:ti,ab OR ikbkb:ti,ab OR map3k14:ti,ab OR relb:ti,ab OR msn:ti,ab OR tfrc:ti,ab OR wipf1:ti,ab OR arpc1b:ti,ab OR atm:ti,ab OR nbs1:ti,ab OR blm:ti,ab OR recql3:ti,ab OR dnmt3b:ti,ab OR zbtb24:ti,ab OR cdca7:ti,ab OR hells:ti,ab OR pms2:ti,ab OR rnf168:ti,ab OR mcm4:ti,ab OR pole:ti,ab OR pole2:ti,ab OR lig1:ti,ab OR nsmce3:ti,ab OR ercc6l2:ti,ab OR gins1:ti,ab OR tbx1:ti,ab OR chd7:ti,ab OR sema3e:ti,ab OR foxn1:ti,ab OR 'del10p13-p14':ti,ab OR rmrp:ti,ab OR smarcal1:ti,ab OR mysm1:ti,ab OR rnu4atac:ti,ab OR extl3:ti,ab OR spink5:ti,ab OR pgm3:ti,ab OR dkc1:ti,ab OR nhp2:ti,ab OR nop10:ti,ab OR rtel1:ti,ab OR terc:ti,ab OR tert:ti,ab OR tinf2:ti,ab OR tpp1:ti,ab OR dclre1b:ti,ab OR snm1:ti,ab OR apollo:ti,ab OR parn:ti,ab OR wrap53:ti,ab OR stn1:ti,ab OR ctc1:ti,ab OR samd9:ti,ab OR samd9l:ti,ab OR tcn2:ti,ab OR slc46a1:ti,ab OR mthfd1:ti,ab OR nemo:ti,ab OR ikbkg:ti,ab OR ikba:ti,ab OR nfkbia:ti,ab OR orai1:ti,ab OR stim1:ti,ab OR pnp:ti,ab OR ttc7a:ti,ab OR sp110:ti,ab OR epg5:ti,ab OR hoil1:ti,ab OR rbck1:ti,ab OR hoip1:ti,ab OR rnf31:ti,ab OR ccbe1:ti,ab OR fat4:ti,ab OR stat5b:ti,ab OR kmt2d:ti,ab OR mll2:ti,ab OR kdm6a:ti,ab OR btk:ti,ab OR ighm:ti,ab OR igll1:ti,ab OR cd79a:ti,ab OR cd79b:ti,ab OR blnk:ti,ab OR tcf3:ti,ab OR 'pik3cd gof':ti,ab OR pik3r1:ti,ab OR pten:ti,ab OR cd19:ti,ab OR cd81:ti,ab OR ms4a1:ti,ab OR cr2:ti,ab OR tnfrsf13b:ti,ab OR taci:ti,ab OR tnfrsf13c:ti,ab OR 'baff-r':ti,ab OR tnfsf12:ti,ab OR mogs:ti,ab OR gcs1:ti,ab OR trnt1:ti,ab OR ttc37:ti,ab OR nfkb1:ti,ab OR nfkb2:ti,ab OR ikzf1:ti,ab OR irf2bp2:ti,ab OR atp6ap1:ti,ab OR aicda:ti,ab OR ung:ti,ab OR ino80:ti,ab OR msh6:ti,ab OR 14q32:ti,ab OR igkc:ti,ab OR card11:ti,ab OR prf1:ti,ab OR unc13d:ti,ab OR stx11:ti,ab OR stxbp2:ti,ab OR faap24:ti,ab OR lyst:ti,ab OR rab27a:ti,ab OR ap3b1:ti,ab OR ap3d1:ti,ab OR foxp3:ti,ab OR il2ra:ti,ab OR ctla4:ti,ab OR lrba:ti,ab OR stat3:ti,ab OR bach2:ti,ab OR aire:ti,ab OR itch:ti,ab OR zap70:ti,ab OR tpp2:ti,ab OR pepd:ti,ab OR tnfrsf6:ti,ab OR faslg:ti,ab OR casp10:ti,ab OR casp8:ti,ab OR fadd:ti,ab OR il10:ti,ab OR il10ra:ti,ab OR il10rb:ti,ab OR nfat5:ti,ab OR sh2d1a:ti,ab OR xiap:ti,ab OR cd27:ti,ab OR ctps1:ti,ab OR rasgrp1:ti,ab OR cd70:ti,ab OR tnfsf7:ti,ab OR rltpr:ti,ab OR itk:ti,ab OR magt1:ti,ab OR prkcd:ti,ab OR elane:ti,ab OR gfi1:ti,ab OR hax1:ti,ab OR g6pc3:ti,ab OR vps45:ti,ab OR g6pt1:ti,ab OR

'wiskott aldrich syndrome':ti,ab OR lamtor2:ti,ab OR taz:ti,ab OR vps13b:ti,ab OR usb1:ti,ab OR jagn1:ti,ab OR clpb:ti,ab OR csf3r:ti,ab OR smarcd2:ti,ab OR hyou1:ti,ab OR itgb2:ti,ab OR slc35c1:ti,ab OR fermt3:ti,ab OR rac2:ti,ab OR actb:ti,ab OR fpr1:ti,ab OR ctsc:ti,ab OR cebpe:ti,ab OR sbds:ti,ab OR wdr1:ti,ab OR cftr:ti,ab OR dnajc21:ti,ab OR mkl1:ti,ab OR cyba:ti,ab OR ncf1:ti,ab OR ncf2:ti,ab OR ncf4:ti,ab OR g6pd:ti,ab OR gata2:ti,ab OR csf2rb:ti,ab OR csf2ra:ti,ab OR il12rb1:ti,ab OR il12b:ti,ab OR ifngr1:ti,ab OR ifngr2:ti,ab OR cybb:ti,ab OR irf8:ti,ab OR tyk2:ti,ab OR isg15:ti,ab OR rorc:ti,ab OR jak1:ti,ab OR tmc6:ti,ab OR tmc8:ti,ab OR cxcr4:ti,ab OR stat2:ti,ab OR irf7:ti,ab OR ifnar2:ti,ab OR fcgr3a:ti,ab OR tlr3:ti,ab OR unc93b1:ti,ab OR traf3:ti,ab OR ticam1:ti,ab OR tbk1:ti,ab OR irf3:ti,ab OR card9:ti,ab OR il17ra:ti,ab OR il17rc:ti,ab OR il17f:ti,ab OR stat1:ti,ab OR traf3ip2:ti,ab OR irak4:ti,ab OR myd88:ti,ab OR irak1:ti,ab OR tirap:ti,ab OR rpsa:ti,ab OR hmox:ti,ab OR apol1:ti,ab OR nbas:ti,ab OR ranbp2:ti,ab OR clcn7:ti,ab OR snx10:ti,ab OR ostm1:ti,ab OR plekhm1:ti,ab OR tcirg1:ti,ab OR tnfrsf11a:ti,ab OR tnfsf11:ti,ab OR ncstn:ti,ab OR psen:ti,ab OR psenen:ti,ab OR trex1:ti,ab OR rnaseh2b:ti,ab OR rnaseh2c:ti,ab OR rnaseh2a:ti,ab OR samhd1:ti,ab OR adar1:ti,ab OR ifih1:ti,ab OR acp5:ti,ab OR tmem173:ti,ab OR pola1:ti,ab OR usp18:ti,ab OR psmb8:ti,ab OR mefv:ti,ab OR mvk:ti,ab OR nalp3:ti,ab OR cias1:ti,ab OR pypaf1:ti,ab OR nlrp12:ti,ab OR nlrp3:ti,ab OR nlrc4:ti,ab OR plcg2:ti,ab OR nlrp1:ti,ab OR tnfrsf1a:ti,ab OR pstpip1:ti,ab OR c2bp1:ti,ab OR nod2:ti,ab OR card15:ti,ab OR adam17:ti,ab OR lpin2:ti,ab OR il1rn:ti,ab OR il36rn:ti,ab OR slc29a3:ti,ab OR card14:ti,ab OR sh3bp2:ti,ab OR copa:ti,ab OR otulin:ti,ab OR tnfaip3:ti,ab OR cecr1:ti,ab OR ap1s3:ti,ab OR c1qa:ti,ab OR c1qb:ti,ab OR c1qc:ti,ab OR c1r:ti,ab OR c1s:ti,ab OR c4a+c4b:ti,ab OR c2:ti,ab OR c3:ti,ab OR c4:ti,ab OR c5:ti,ab OR c6:ti,ab OR c7:ti,ab OR c8a:ti,ab OR c8g:ti,ab OR c8b:ti,ab OR c9:ti,ab OR masp2:ti,ab OR fcn3:ti,ab OR serping1:ti,ab OR cfb:ti,ab OR cfd:ti,ab OR cfp:ti,ab OR cfi:ti,ab OR cfh:ti,ab OR cfhr:ti,ab OR thbd:ti,ab OR cd46:ti,ab OR cd59:ti,ab OR cd55:ti,ab OR pid:ti,ab OR c1q:ti,ab

#3: 1296 results
#1 AND #2

#4: 524 results
#1 AND #2 NOT ('human immunodeficiency virus'/exp OR 'human immunodeficiency virus infection'/exp) NOT ([animals]/lim NOT [humans]/lim) AND ([english]/lim OR [german]/lim OR [french]/lim OR [italian]/lim) NOT [conference abstract]/lim

11.2. Appendix B – Search terms used for MEDLINE

#1: 52710 results
(((fatal or death or lethal or deadly or severe or recurrent or died or succumbed or deceased or expired or passed away or perished) and (infection* or infected or infectious disease* or inflammat* or seps* or septic or bacteremia* or abscess* or pulmonary infection* or pneumonia or mastoidit* or sinusit* or otit* or epiglottit* or meningit* or encephalit* or endocardit* or catheter-related or line-related or chronic diarreha* or peritonit* or cholecystit* or cholangit* or urinary tract infection* or cellulit* or necrotising fasciit* or necrotizing fasciit* or myonecros* or impetigo or folliculit* or osteomylit*)).ti,ab. or exp Infection/ or exp Inflammation/ or exp Respiratory Insufficiency/ or respiratory failure.ti,ab.) and (exp Mortality/ or exp Autopsy/ or exp Death/)

#2: 386144 results
(il2rg or jak3 or il7r or ptprc or cd3d or cd3e or cd247 or coro1a or lat or rag1 or rag2 or dclre1c or prkdc or nhej1 or lig4 or ak2 or ada or dock2 or cd40lg or tnfsf5 or cd40 or tnfrsf5 or icos or cd3g or cd8a or tap1 or tap2 or tapbp or b2m or ciita or rfxank or rfx5 or rfxap or dock8 or rhoh or stk4 or trac or lck or malt1 or bcl10 or bcl11b or il21 or il21r or tnfrsf4 or ikbkb or map3k14 or relb or msn or tfrc or wipf1 or arpc1b or atm or nbs1 or blm or recql3 or dnmt3b or zbtb24 or cdca7 or hells or pms2 or rnf168 or mcm4 or pole or pole2 or lig1 or nsmce3 or ercc6l2 or gins1 or tbx1 or chd7 or sema3e or foxn1 or del10p13- p14 or rmrp or smarcal1 or mysm1 or rnu4atac or extl3 or spink5 or pgm3 or dkc1 or nhp2 or nop10 or rtel1 or terc or tert or tinf2 or tpp1 or dclre1b or snm1 or apollo or parn or wrap53 or stn1 or ctc1 or samd9 or samd9l or tcn2 or slc46a1 or mthfd1 or nemo or ikbkg or ikba or nfkbia or orai1 or stim1 or pnp or ttc7a or sp110 or epg5 or hoil1 or rbck1 or hoip1 or rnf31 or ccbe1 or fat4 or stat5b or kmt2d or mll2 or kdm6a or btk or ighm or igll1 or cd79a or cd79b or blnk or tcf3 or pik3cd gof or pik3r1 or pten or cd19 or cd81 or ms4a1 or cr2 or tnfrsf13b or taci or tnfrsf13c or baff-r or tnfsf12 or mogs or gcs1 or trnt1 or ttc37 or nfkb1 or nfkb2 or ikzf1 or irf2bp2 or atp6ap1 or aicda or ung or ino80 or msh6 or 14q32 or igkc or card11 or prf1 or unc13d or stx11 or stxbp2 or faap24 or lyst or rab27a or ap3b1 or ap3d1 or foxp3 or il2ra or ctla4 or lrba or stat3 or bach2 or aire or itch or zap70 or tpp2 or pepd or tnfrsf6 or faslg or casp10 or casp8 or fadd or il10 or il10ra or il10rb or nfat5 or sh2d1a or xiap or cd27 or ctps1 or rasgrp1 or cd70 or tnfsf7 or rltpr or itk or magt1 or prkcd or elane or gfi1 or hax1 or g6pc3 or vps45 or g6pt1 or wiskott aldrich syndrome or lamtor2 or taz or vps13b or usb1 or jagn1 or clpb or csf3r or smarcd2 or hyou1 or itgb2 or slc35c1 or fermt3 or rac2 or actb or fpr1 or ctsc or cebpe or sbds or wdr1 or cftr or dnajc21 or mkl1 or cyba or ncf1 or ncf2 or ncf4 or g6pd or gata2 or csf2rb or csf2ra or il12rb1 or il12b or ifngr1 or ifngr2 or cybb or irf8 or tyk2 or isg15 or rorc or jak1 or tmc6 or tmc8 or cxcr4 or stat2 or irf7 or ifnar2 or fcgr3a or tlr3 or unc93b1 or traf3 or ticam1 or tbk1 or irf3 or card9 or il17ra or il17rc or il17f or stat1 or traf3ip2 or irak4 or myd88 or irak1 or tirap or rpsa or hmox or apol1 or nbas or ranbp2 or clcn7 or snx10 or ostm1 or plekhm1 or tcirg1 or tnfrsf11a or tnfsf11 or ncstn or psen or psenen or trex1 or rnaseh2b or rnaseh2c or rnaseh2a or samhd1 or adar1 or ifih1 or acp5 or tmem173 or pola1 or usp18 or psmb8 or mefv or mvk or nalp3 or cias1 or pypaf1 or nlrp12 or nlrp3 or nlrc4 or plcg2 or nlrp1 or tnfrsf1a or pstpip1 or c2bp1 or nod2 or card15 or adam17 or lpin2 or il1rn or il36rn or slc29a3 or card14 or sh3bp2 or copa or otulin or tnfaip3 or cecr1 or ap1s3 or c1qa or c1qb or c1qc or c1r or c1s or c4a+c4b or c2 or c3 or c4 or c5 or c6 or c7 or c8a or c8g or c8b or c9 or masp2 or fcn3 or serping1 or cfb or cfd or cfp or cfi or cfh or cfhr or thbd or cd46 or cd59 or cd55 or pid or c1q).ti,ab.

#3: 546 results
1 and 2

#4: 457 results
3 not (exp HIV Infections/ or exp HIV/) not (animals not humans).sh.

#5: 432 results
limit 4 to (english or german or french or italian)

11.3. Appendix C – Search terms used for PUBMED

```
(
  (
    (
      (
        (
          (
            fatal[Title/Abstract] OR death[Title/Abstract] OR le-
thal[Title/Abstract] OR deadly[Title/Abstract] OR died[Title/Abstract] OR
succumbed[Title/Abstract] OR deceased[Title/Abstract] OR ex-
pired[Title/Abstract] OR "passed away"[Title/Abstract] OR per-
ished[Title/Abstract] OR fatality[Title/Abstract] OR "cause of death" [Ti-
tle/Abstract] OR autopsy[Title/Abstract]
          )
        )
        AND
        (
          (
            infection* [Title/Abstract] OR infected[Title/Abstract] OR "in-
fectious disease*" [Title/Abstract] OR inflammat*[Title/Abstract] OR
seps*[Title/Abstract] OR septic[Title/Abstract] OR bactere-
mia*[Title/Abstract] OR abscess* [Title/Abstract] OR "pulmonary infec-
tion*"[Title/Abstract] OR pneumonia[Title/Abstract] OR mastoid-
it*[Title/Abstract] OR sinusit* [Title/Abstract] OR otit*[Title/Abstract]
OR epiglottit*[Title/Abstract] OR meningit*[Title/Abstract] OR encepha-
lit*[Title/Abstract] OR endocardit* [Title/Abstract] OR "catheter-
related"[Title/Abstract] OR "line-related" [Title/Abstract] OR "chronic di-
arreha*"[Title/Abstract] OR peritonit* [Title/Abstract] OR chole-
cystit*[Title/Abstract] OR cholangit* [Title/Abstract] OR "urinary tract
infection*"[Title/Abstract] OR cellulit* [Title/Abstract] OR "necrotising
fasciit*"[Title/Abstract] OR "necrotizing fasciit*"[Title/Abstract] OR my-
onecros*[Title/Abstract] OR impetigo[Title/Abstract] OR follicu-
lit*[Title/Abstract] OR osteomylit* [Title/Abstract] OR "respiratory fail-
ure"[Title/Abstract]
          )
        )
      )
      AND
      (
        (
          il2rg[Title/Abstract] OR jak3[Title/Abstract] OR
il7r[Title/Abstract] OR ptprc[Title/Abstract] OR cd3d[Title/Abstract] OR
cd3e[Title/Abstract] OR cd247[Title/Abstract] OR coro1a[Title/Abstract] OR
lat[Title/Abstract] OR rag1[Title/Abstract] OR rag2[Title/Abstract] OR
dclre1c[Title/Abstract] OR prkdc[Title/Abstract] OR nhej1[Title/Abstract]
OR lig4[Title/Abstract] OR ak2[Title/Abstract] OR ada[Title/Abstract] OR
dock2[Title/Abstract] OR cd40lg[Title/Abstract] OR tnfsf5[Title/Abstract]
OR cd40[Title/Abstract] OR tnfrsf5[Title/Abstract] OR icos[Title/Abstract]
OR cd3g[Title/Abstract] OR cd8a[Title/Abstract] OR tap1[Title/Abstract] OR
tap2[Title/Abstract] OR tapbp[Title/Abstract] OR b2m[Title/Abstract] OR
ciita[Title/Abstract] OR rfxank[Title/Abstract] OR rfx5[Title/Abstract] OR
rfxap[Title/Abstract] OR dock8[Title/Abstract] OR rhoh[Title/Abstract] OR
stk4[Title/Abstract] OR trac[Title/Abstract] OR lck[Title/Abstract] OR
malt1[Title/Abstract] OR bcl10[Title/Abstract] OR bcl11b[Title/Abstract] OR
il21[Title/Abstract] OR il21r[Title/Abstract] OR tnfrsf4[Title/Abstract] OR
ikbkb[Title/Abstract] OR map3k14[Title/Abstract] OR relb[Title/Abstract] OR
msn[Title/Abstract] OR tfrc[Title/Abstract] OR wipf1[Title/Abstract] OR
arpc1b[Title/Abstract] OR atm[Title/Abstract] OR nbs1[Title/Abstract] OR
blm[Title/Abstract] OR recql3[Title/Abstract] OR dnmt3b[Title/Abstract] OR
zbtb24[Title/Abstract] OR cdca7[Title/Abstract] OR hells[Title/Abstract] OR
pms2[Title/Abstract] OR rnf168[Title/Abstract] OR mcm4[Title/Abstract] OR
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pole[Title/Abstract] OR pole2[Title/Abstract] OR lig1[Title/Abstract] OR nsmce3[Title/Abstract] OR ercc6l2[Title/Abstract] OR gins1[Title/Abstract] OR tbx1[Title/Abstract] OR chd7[Title/Abstract] OR sema3e[Title/Abstract] OR foxn1[Title/Abstract] OR "del10p13- p14"[Title/Abstract] OR rmrp[Title/Abstract] OR smarcal1[Title/Abstract] OR mysm1[Title/Abstract] OR rnu4atac[Title/Abstract] OR extl3[Title/Abstract] OR spink5[Title/Abstract] OR pgm3[Title/Abstract] OR dkc1[Title/Abstract] OR nhp2[Title/Abstract] OR nop10[Title/Abstract] OR rtel1[Title/Abstract] OR terc[Title/Abstract] OR tert[Title/Abstract] OR tinf2[Title/Abstract] OR tpp1[Title/Abstract] OR dclre1b[Title/Abstract] OR snm1[Title/Abstract] OR apollo[Title/Abstract] OR parn[Title/Abstract] OR wrap53[Title/Abstract] OR stn1[Title/Abstract] OR ctc1[Title/Abstract] OR samd9[Title/Abstract] OR samd9l[Title/Abstract] OR tcn2[Title/Abstract] OR slc46a1[Title/Abstract] OR mthfd1[Title/Abstract] OR nemo[Title/Abstract] OR ikbkg[Title/Abstract] OR ikba[Title/Abstract] OR nfkbia[Title/Abstract] OR orai1[Title/Abstract] OR stim1[Title/Abstract] OR pnp[Title/Abstract] OR ttc7a[Title/Abstract] OR sp110[Title/Abstract] OR epg5[Title/Abstract] OR hoil1[Title/Abstract] OR rbck1[Title/Abstract] OR hoip1[Title/Abstract] OR rnf31[Title/Abstract] OR ccbe1[Title/Abstract] OR fat4[Title/Abstract] OR stat5b[Title/Abstract] OR kmt2d[Title/Abstract] OR mll2[Title/Abstract] OR kdm6a[Title/Abstract] OR btk[Title/Abstract] OR ighm[Title/Abstract] OR igll1[Title/Abstract] OR cd79a[Title/Abstract] OR cd79b[Title/Abstract] OR blnk[Title/Abstract] OR tcf3[Title/Abstract] OR "pik3cd gof"[Title/Abstract] OR pik3r1[Title/Abstract] OR pten[Title/Abstract] OR cd19[Title/Abstract] OR cd81[Title/Abstract] OR ms4a1[Title/Abstract] OR cr2[Title/Abstract] OR tnfrsf13b[Title/Abstract] OR taci[Title/Abstract] OR tnfrsf13c[Title/Abstract] OR "baff-r"[Title/Abstract] OR tnfsf12[Title/Abstract] OR mogs[Title/Abstract] OR gcs1[Title/Abstract] OR trnt1[Title/Abstract] OR ttc37[Title/Abstract] OR nfkb1[Title/Abstract] OR nfkb2[Title/Abstract] OR ikzf1[Title/Abstract] OR irf2bp2[Title/Abstract] OR atp6ap1[Title/Abstract] OR aicda[Title/Abstract] OR ung[Title/Abstract] OR ino80[Title/Abstract] OR msh6[Title/Abstract] OR 14q32[Title/Abstract] OR igkc[Title/Abstract] OR card11[Title/Abstract] OR prf1[Title/Abstract] OR unc13d[Title/Abstract] OR stx11[Title/Abstract] OR stxbp2[Title/Abstract] OR faap24[Title/Abstract] OR lyst[Title/Abstract] OR rab27a[Title/Abstract] OR ap3b1[Title/Abstract] OR ap3d1[Title/Abstract] OR foxp3[Title/Abstract] OR il2ra[Title/Abstract] OR ctla4[Title/Abstract] OR lrba[Title/Abstract] OR stat3[Title/Abstract] OR bach2[Title/Abstract] OR aire[Title/Abstract] OR itch[Title/Abstract] OR zap70[Title/Abstract] OR tpp2[Title/Abstract] OR pepd[Title/Abstract] OR tnfrsf6[Title/Abstract] OR faslg[Title/Abstract] OR casp10[Title/Abstract] OR casp8[Title/Abstract] OR fadd[Title/Abstract] OR il10[Title/Abstract] OR il10ra[Title/Abstract] OR il10rb[Title/Abstract] OR nfat5[Title/Abstract] OR sh2d1a[Title/Abstract] OR xiap[Title/Abstract] OR cd27[Title/Abstract] OR ctps1[Title/Abstract] OR rasgrp1[Title/Abstract] OR cd70[Title/Abstract] OR tnfsf7[Title/Abstract] OR rltpr[Title/Abstract] OR itk[Title/Abstract] OR magt1[Title/Abstract] OR prkcd[Title/Abstract] OR elane[Title/Abstract] OR gfi1[Title/Abstract] OR hax1[Title/Abstract] OR g6pc3[Title/Abstract] OR vps45[Title/Abstract] OR g6pt1[Title/Abstract] OR "wiskott aldrich syndrome"[Title/Abstract] OR lamtor2[Title/Abstract] OR taz[Title/Abstract] OR vps13b[Title/Abstract] OR usb1[Title/Abstract] OR jagn1[Title/Abstract] OR clpb[Title/Abstract] OR csf3r[Title/Abstract] OR smarcd2[Title/Abstract] OR hyou1[Title/Abstract] OR itgb2[Title/Abstract] OR slc35c1[Title/Abstract] OR fermt3[Title/Abstract] OR rac2[Title/Abstract] OR actb[Title/Abstract] OR fpr1[Title/Abstract] OR ctsc[Title/Abstract] OR cebpe[Title/Abstract] OR sbds[Title/Abstract] OR wdr1[Title/Abstract] OR cftr[Title/Abstract] OR dnajc21[Title/Abstract] OR mkl1[Title/Abstract] OR cyba[Title/Abstract] OR ncf1[Title/Abstract] OR ncf2[Title/Abstract] OR ncf4[Title/Abstract] OR g6pd[Title/Abstract] OR gata2[Title/Abstract] OR csf2rb[Title/Abstract] OR csf2ra[Title/Abstract] OR il12rb1[Title/Abstract] OR il12b[Title/Abstract] OR ifngr1[Title/Abstract] OR ifngr2[Title/Abstract] OR cybb[Title/Abstract] OR irf8[Title/Abstract] OR tyk2[Title/Abstract] OR isg15[Title/Abstract] OR rorc[Title/Abstract] OR jak1[Title/Abstract] OR tmc6[Title/Abstract] OR tmc8[Title/Abstract] OR cxcr4[Title/Abstract] OR stat2[Title/Abstract] OR

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irf7[Title/Abstract] OR ifnar2[Title/Abstract] OR fcgr3a[Title/Abstract] OR
tlr3[Title/Abstract] OR unc93b1[Title/Abstract] OR traf3[Title/Abstract] OR
ticam1[Title/Abstract] OR tbk1[Title/Abstract] OR irf3[Title/Abstract] OR
card9[Title/Abstract] OR il17ra[Title/Abstract] OR il17rc[Title/Abstract]
OR il17f[Title/Abstract] OR stat1[Title/Abstract] OR
traf3ip2[Title/Abstract] OR irak4[Title/Abstract] OR myd88[Title/Abstract]
OR irak1[Title/Abstract] OR tirap[Title/Abstract] OR rpsa[Title/Abstract]
OR hmox[Title/Abstract] OR apol1[Title/Abstract] OR nbas[Title/Abstract] OR
ranbp2[Title/Abstract] OR clcn7[Title/Abstract] OR snx10[Title/Abstract] OR
ostm1[Title/Abstract] OR plekhm1[Title/Abstract] OR tcirg1[Title/Abstract]
OR tnfrsf11a[Title/Abstract] OR tnfsf11[Title/Abstract] OR
ncstn[Title/Abstract] OR psen[Title/Abstract] OR psenen[Title/Abstract] OR
trex1[Title/Abstract] OR rnaseh2b[Title/Abstract] OR
rnaseh2c[Title/Abstract] OR rnaseh2a[Title/Abstract] OR
samhd1[Title/Abstract] OR adar1[Title/Abstract] OR ifih1[Title/Abstract] OR
acp5[Title/Abstract] OR tmem173[Title/Abstract] OR pola1[Title/Abstract] OR
usp18[Title/Abstract] OR psmb8[Title/Abstract] OR mefv[Title/Abstract] OR
mvk[Title/Abstract] OR nalp3[Title/Abstract] OR cias1[Title/Abstract] OR
pypaf1[Title/Abstract] OR nlrp12[Title/Abstract] OR nlrp3[Title/Abstract]
OR nlrc4[Title/Abstract] OR plcg2[Title/Abstract] OR nlrp1[Title/Abstract]
OR tnfrsf1a[Title/Abstract] OR pstpip1[Title/Abstract] OR
c2bp1[Title/Abstract] OR nod2[Title/Abstract] OR card15[Title/Abstract] OR
adam17[Title/Abstract] OR lpin2[Title/Abstract] OR il1rn[Title/Abstract] OR
il36rn[Title/Abstract] OR slc29a3[Title/Abstract] OR card14[Title/Abstract]
OR sh3bp2[Title/Abstract] OR copa[Title/Abstract] OR otulin[Title/Abstract]
OR tnfaip3[Title/Abstract] OR cecr1[Title/Abstract] OR
ap1s3[Title/Abstract] OR c1qa[Title/Abstract] OR c1qb[Title/Abstract] OR
c1qc[Title/Abstract] OR c1r[Title/Abstract] OR c1s[Title/Abstract] OR
"c4a+c4b"[Title/Abstract] OR c2[Title/Abstract] OR c3[Title/Abstract] OR
c4[Title/Abstract] OR c5[Title/Abstract] OR c6[Title/Abstract] OR
c7[Title/Abstract] OR c8a[Title/Abstract] OR c8g[Title/Abstract] OR
c8b[Title/Abstract] OR c9[Title/Abstract] OR masp2[Title/Abstract] OR
fcn3[Title/Abstract] OR serping1[Title/Abstract] OR cfb[Title/Abstract] OR
cfd[Title/Abstract] OR cfp[Title/Abstract] OR cfi[Title/Abstract] OR
cfh[Title/Abstract] OR cfhr[Title/Abstract] OR thbd[Title/Abstract] OR
cd46[Title/Abstract] OR cd59[Title/Abstract] OR cd55[Title/Abstract] OR
pid[Title/Abstract] OR c1q[Title/Abstract]
        )
      )
    )
    NOT
    (
      mouse[Title/Abstract] OR mice[Title/Abstract] OR ani-
mal*[Title/Abstract] OR "cell line*" [Title/Abstract] OR "cell
death"[Title/Abstract] OR "programmed death" [Title/Abstract]
    )
  )
  NOT hiv[Title]
)
AND
(
  (
    (
      inprocess[sb]
    )
    OR
    (
      publisher[sb] NOT pubstatusnihms NOT pubstatuspmcsd NOT pmcbook
    )
  )
)
```

11.4. Appendix D – Search terms used for SCOPUS

```
(
  (
    TITLE-ABS
    (
      fatal OR death OR lethal OR deadly OR died OR succumbed OR deceased
OR expired OR "passed away" OR perished OR fatality OR "cause of death" OR
autopsy
    )
  )
  AND
  (
    TITLE-ABS
    (
      infection* OR infected OR "infectious disease*" OR inflammat* OR
seps* OR septic OR bacteremia* OR abscess* OR "pumonary infection*" OR
pneumonia OR mastoidit* OR sinusit* OR otit* OR epiglottit* OR meningit* OR
encephalit* OR endocardit* OR "catheter-related" OR "line-related" OR
"chronic diarreha*" OR peritonit* OR chlocystit* OR cholangit* OR "urinary
tract infection*" OR cellulit* OR "necrotising fasciit*" OR "necrotizing
fasciit*" OR myonecros* OR impetigo OR folliculit* OR osteomylit* OR "res-
piratory failure"
    )
  )
)
AND
(
  TITLE-ABS
  (
    il2rg OR jak3 OR il7r OR ptprc OR cd3d OR cd3e OR cd247 OR coro1a OR
lat OR rag1 OR rag2 OR dclre1c OR prkdc OR nhej1 OR lig4 OR ak2 OR ada OR
dock2 OR cd40lg OR tnfsf5 OR cd40 OR tnfrsf5 OR icos OR cd3g OR cd8a OR
tap1 OR tap2 OR tapbp OR b2m OR ciita OR rfxank OR rfx5 OR rfxap OR dock8
OR rhoh OR stk4 OR trac OR lck OR malt1 OR bcl10 OR bcl11b OR il21 OR il21r
OR tnfrsf4 OR ikbkb OR map3k14 OR relb OR msn OR tfrc OR wipf1 OR arpc1b OR
atm OR nbs1 OR blm OR recql3 OR dnmt3b OR zbtb24 OR cdca7 OR hells OR pms2
OR rnf168 OR mcm4 OR pole OR pole2 OR lig1 OR nsmce3 OR ercc6l2 OR gins1 OR
tbx1 OR chd7 OR sema3e OR foxn1 OR "del10p13-p14" OR rmrp OR smarcal1 OR
mysm1 OR rnu4atac OR extl3 OR spink5 OR pgm3 OR dkc1 OR nhp2 OR nop10 OR
rtel1 OR terc OR tert OR tinf2 OR tpp1 OR dclre1b OR snm1 OR apollo OR parn
OR wrap53 OR stn1 OR ctc1 OR samd9 OR samd9l OR tcn2 OR slc46a1 OR mthfd1
OR nemo OR ikbkg OR ikba OR nfkbia OR orai1 OR stim1 OR pnp OR ttc7a OR
sp110 OR epg5 OR hoil1 OR rbck1 OR hoip1 OR rnf31 OR ccbe1 OR fat4 OR
stat5b OR kmt2d OR mll2 OR kdm6a OR btk OR ighm OR igll1 OR cd79a OR cd79b
OR blnk OR tcf3 OR "pik3cd gof" OR pik3r1 OR pten OR cd19 OR cd81 OR ms4a1
OR cr2 OR tnfrsf13b OR taci OR tnfrsf13c OR "baff-r" OR tnfsf12 OR mogs OR
gcs1 OR trnt1 OR ttc37 OR nfkb1 OR nfkb2 OR ikzf1 OR irf2bp2 OR atp6ap1 OR
aicda OR ung OR ino80 OR msh6 OR 14q32 OR igkc OR card11 OR prf1 OR unc13d
OR stx11 OR stxbp2 OR faap24 OR lyst OR rab27a OR ap3b1 OR ap3d1 OR foxp3
OR il2ra OR ctla4 OR lrba OR stat3 OR bach2 OR aire OR itch OR zap70 OR
tpp2 OR pepd OR tnfrsf6 OR faslg OR casp10 OR casp8 OR fadd OR il10 OR
il10ra OR il10rb OR nfat5 OR sh2d1a OR xiap OR cd27 OR ctps1 OR rasgrp1 OR
cd70 OR tnfsf7 OR rltpr OR itk OR magt1 OR prkcd OR elane OR gfi1 OR hax1
OR g6pc3 OR vps45 OR g6pt1 OR "wiskott aldrich syndrome" OR lamtor2 OR taz
OR vps13b OR usb1 OR jagn1 OR clpb OR csf3r OR smarcd2 OR hyou1 OR itgb2 OR
slc35c1 OR fermt3 OR rac2 OR actb OR fpr1 OR ctsc OR cebpe OR sbds OR wdr1
OR cftr OR dnajc21 OR mkl1 OR cyba OR ncf1 OR ncf2 OR ncf4 OR g6pd OR gata2
OR csf2rb OR csf2ra OR il12rb1 OR il12b OR ifngr1 OR ifngr2 OR cybb OR irf8
OR tyk2 OR isg15 OR rorc OR jak1 OR tmc6 OR tmc8 OR cxcr4 OR stat2 OR irf7
OR ifnar2 OR fcgr3a OR tlr3 OR unc93b1 OR traf3 OR ticam1 OR tbk1 OR irf3
OR card9 OR il17ra OR il17rc OR il17f OR stat1 OR traf3ip2 OR irak4 OR
myd88 OR irak1 OR tirap OR rpsa OR hmox OR apol1 OR nbas OR ranbp2 OR clcn7
```

```
OR snx10 OR ostm1 OR plekhm1 OR tcirg1 OR tnfrsf11a OR tnfsf11 OR ncstn OR
psen OR psenen OR trex1 OR rnaseh2b OR rnaseh2c OR rnaseh2a OR samhd1 OR
adar1 OR ifih1 OR acp5 OR tmem173 OR pola1 OR usp18 OR psmb8 OR mefv OR mvk
OR nalp3 OR cias1 OR pypaf1 OR nlrp12 OR nlrp3 OR nlrc4 OR plcg2 OR nlrp1
OR tnfrsf1a OR pstpip1 OR c2bp1 OR nod2 OR card15 OR adam17 OR lpin2 OR
il1rn OR il36rn OR slc29a3 OR card14 OR sh3bp2 OR copa OR otulin OR tnfaip3
OR cecr1 OR ap1s3 OR c1qa OR c1qb OR c1qc OR c1r OR c1s OR c4a+c4b OR c2 OR
c3 OR c4 OR c5 OR c6 OR c7 OR c8a OR c8g OR c8b OR c9 OR masp2 OR fcn3 OR
serping1 OR cfb OR cfd OR cfp OR cfi OR cfh OR cfhr OR thbd OR cd46 OR cd59
OR cd55 OR pid OR c1q
  )
)
AND NOT
(
  TITLE-ABS-KEY
  (
    mouse OR mice OR animals* OR "cell line*" OR "cell death" OR "pro-
grammed death"
  )
)
AND NOT
(
  TITLE
  (
    hiv
  )
)
AND
(
  LIMIT-TO
  (
    LANGUAGE, "English"
  )
  OR
  LIMIT-TO
  (
    LANGUAGE, "German"
  )
  OR
  LIMIT-TO
  (
    LANGUAGE, "French"
  )
  OR
  LIMIT-TO
  (
    LANGUAGE, "Italian"
  )
)
```

11.5. Appendix E – List of PID related genes/terms used for search queries

14Q32	CD55	G6PT1	LPIN2	PSEN	TAP2
ACP5	CD59	**GATA2**	**LRBA**	PSENEN	TAPBP
ACTB	CD70	GCS1	**LYST**	PSMB8	TAZ
ADA	CD79A	GFI1	**MAGT1**	PSTPIP1	TBK1
ADAM17	CD79B	GINS1	MALT1	PTEN	TBX1
ADAR1	CD81	HAX1	MAP3K14	PTPRC	TCF3
AICDA	CD247	HELLS	MASP2	PYPAF1	TCIRG1
AIRE	CDCA7	HMOX	MCM4	**RAB27A**	TCN2
AK2	CEBPE	HOIL1	MEFV	**RAC2**	TERC
AP1S3	**CECR1**	HOIP1	MKL1	**RAG1**	TERT
AP3B1	CFB	HYOU1	MLL2	**RAG2**	TFRC
AP3D1	CFD	**ICOS**	MOGS	RANBP2	THBD
APOL1	CFH	IFIH1	MS4A1	RASGRP1	TICAM1
APOLLO	CFHR	IFNAR2	MSH6	RBCK1	TINF2
ARPC1B	CFI	**IFNGR1**	MSN	RECQL3	TIRAP
ATM	**CFP**	**IFNGR2**	MTHFD1	RELB	TLR3
ATP6AP1	CFTR	IGHM	MVK	RFX5	TMC6
B2M	CHD7	IGKC	MYD88	RFXANK	TMC8
BACH2	CIAS1	IGLL1	MYSM1	RFXAP	TMEM173
'BAFF-R'	CIITA	IKBA	NALP3	RHOH	TNFAIP3
BCL10	CLCN7	**IKBKB**	NBAS	RLTPR	TNFRSF1A
BCL11B	CLPB	**IKBKG**	NBS1	**RMRP**	TNFRSF4
BLM	COPA	IKZF1	NCF1	RNASEH2A	TNFRSF5
BLNK	CORO1A	IL1RN	**NCF2**	RNASEH2B	TNFRSF6
BTK	CR2	IL2RA	NCF4	RNASEH2C	TNFRSF11A
C1Q	CSF2RA	**IL2RG**	NCSTN	RNF168	TNFRSF13B
C1QA	CSF2RB	IL36RN	NEMO	RNF31	TNFRSF13C
C1QB	CSF3R	IL7R	NFAT5	RNU4ATAC	TNFSF11
C1QC	CTC1	IL10	NFKB1	RORC	TNFSF12
C1R	CTLA4	IL10RA	NFKB2	RPSA	TNFSF5
C1S	CTPS1	IL10RB	**NFKBIA**	**RTEL1**	TNFSF7
C2	CTSC	**IL12B**	NHEJ1	SAMD9	TPP1
C2BP1	**CXCR4**	**IL12RB1**	NHP2	SAMD9L	TPP2
C3	CYBA	IL17F	NLRC4	SAMHD1	TRAC
C4	**CYBB**	**IL17RA**	NLRP1	SBDS	TRAF3
C4A+C4B	DCLRE1B	IL17RC	NLRP12	SEMA3E	TRAF3IP2
C5	**DCLRE1C**	IL21	NLRP3	SERPING1	TREX1
C6	'DEL10P13-P14'	IL21R	NOD2	**SH2D1A**	**TRNT1**
C7	**DKC1**	INO80	NOP10	SH3BP2	**TTC37**
C8A	DNAJC21	IRAK1	NSMCE3	SLC29A3	TTC7A
C8B	**DNMT3B**	**IRAK4**	ORAI1	SLC35C1	TYK2
C8G	**DOCK2**	IRF2BP2	OSTM1	SLC46A1	**UNC13D**
C9	**DOCK8**	IRF3	OTULIN	SMARCAL1	UNC93B1
CARD9	ELANE	IRF7	PARN	SMARCD2	UNG
CARD11	EPG5	IRF8	PEPD	SNM1	USB1
CARD14	ERCC6L2	ISG15	**PGM3**	SNX10	USP18
CARD15	EXTL3	ITCH	**PID**	SP110	VPS13B
CASP8	**FAAP24**	**ITGB2**	'PIK3CD GOF'	SPINK5	VPS45
CASP10	FADD	**ITK**	**PIK3R1**	**STAT1**	**WDR1**
CCBE1	FASLG	JAGN1	PLCG2	STAT2	WIPF1
CD8A	FAT4	JAK1	PLEKHM1	**STAT3**	**'WISKOTT ALDRICH SYNDROME'**
CD19	FCGR3A	JAK3	PMS2	STAT5B	
CD27	FCN3	KDM6A	**PNP**	STIM1	
CD3D	FERMT3	KMT2D	POLA1	STK4	WRAP53
CD3E	FOXN1	LAMTOR2	POLE	STN1	**XIAP**
CD3G	**FOXP3**	LAT	POLE2	STX11	**ZAP70**
CD40	FPR1	LCK	**PRF1**	STXBP2	**ZBTB24**
CD40LG	G6PC3	LIG1	PRKCD	TACI	
CD46	G6PD	LIG4	PRKDC	TAP1	

The 64 PID genes that were encountered in eligible extracted case reports and the general search term PID are marked in bold.

'WISKOTT ALDRICH SYNDROME' was chosen instead of WAS, because the word *what* in German is identical with this acronym.

GOF in PIK3CD GOF means *gain of function*.

BAFF-R is synonymous with TNFRSF13C.

14Q32 and DEL10P13-P14 refer to mutations on chromosomal level.

11.6. Appendix F – Table 8: Consulted full-text articles

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R1	**Abe K, Endo Y et al.**	Unique phenotypes of C1s deficiency and abnormality caused by two compound heterozygosities in a Japanese family	2009	Journal of Immunology 182(3): 1681-1688 doi:10.4049/jimmunol.182.3.1681	0	0	no infectious agent identified
R2	**Aeschlimann FA, Batu ED et al.**	A20 haploinsufficiency (HA20): clinical phenotypes and disease course of patients with a newly recognised NF-kB-mediated autoinflammatory disease	2018	Ann Rheum Dis 77(5): 728-735 doi:10.1136/annrheumdis-2017-212403	0	0	no infectious agent mentioned
R3	**Aghamohammadi A, Imai K et al.**	Ataxia-telangiectasia in a patient presenting with hyper-immunoglobulin M syndrome	2010	Journal of Investigational Allergology & Clinical Immunology 20(5): 442-445	0	0	no infectious agent mentioned
R4	**Aghamohammadi A, Moghaddam Z et al.**	Investigation of underlying primary immunodeficiencies in patients with severe atopic dermatitis	2014	Allergologia et Immunopathologia 42(4): 336-341 doi:10.1016/j.aller.2013.02.004	0	0	no individual patients data and no mutation status
R5	**Ailal F, Bousfiha AA et al.**	Griscelli syndrome: About one case	2004	Nouvelles Dermatologiques 23(4): 218-220	0	0	no infectious agent mentioned
R6	**Aiuti A, Cattaneo F et al.**	Gene therapy for immunodeficiency due to adenosine deaminase deficiency	2009	New England Journal of Medicine 360(5): 447-458 doi:10.1056/NEJMoa0805817	0	0	no fatality mentioned
R7	**Akar HH, Patiroglu T et al.**	Combined immunodeficiencies: Twenty years experience from a single center in Turkey	2016	Central European Journal of Immunology 41(1): 107-115 doi:10.5114/ceji.2015.56168	4	0	(1 additional case with questionable link between intracranial haemorrhage post-HSCT and EBV + CMV infection)
R8	**Al-Herz W & Moussa MAA**	Survival and predictors of death among primary immunodeficient patients: A registry-based study	2012	Journal of Clinical Immunology 32(3): 467-473 doi:10.1007/s10875-011-9636-1	0	0	no individual patient data
R9	**Al-Saud B, Al-Mousa H et al.**	Primary Immunodeficiency Diseases in Saudi Arabia: a Tertiary Care Hospital Experience over a Period of Three Years (2010–2013)	2015	Journal of Clinical Immunology 35(7): 651-660 doi:10.1007/s10875-015-0197-6	0	0	no individual patient data
R10	**Al-Saud BK, Al-Sum Z et al.**	Clinical, immunological, and molecular characterization of Hyper-IgM syndrome due to CD40 deficiency in eleven patients	2013	Journal of Clinical Immunology 33(8): 1325-1335 doi:10.1007/s10875-013-9951-9	2	0	
R11	**Aleinikova OV, Fedorova AS & Sharapova SO**	Should allogeneic hematopoietic stem cell transplantation be a treatment option for patients with Nijmegen breakage syndrome? Belarusian experience	2015	Cellular Therapy and Transplantation 4(1-2): 31-36 doi:10.18620/1866-8836-2015-4-1-2-31-37	0	0	no individual patient data
R12	**Alkhairy OK, Abolhassani H et al.**	Spectrum of Phenotypes Associated with Mutations in LRBA	2016	Journal of Clinical Immunology 36(1): 33-45 doi:10.1007/s10875-015-0224-7	0	0	either infectious agent missing or no mention of fatality
R13	**Alkhairy OK, Perez-Becker R et al.**	Novel mutations in TNFRSF7/CD27: Clinical, immunologic, and genetic characterization of human CD27 deficiency	2015	Journal of Allergy and Clinical Immunology 136(3): 703-712.e710 doi:10.1016/j.jaci.2015.02.022	5	0	
R14	**Alkhairy OK, Rezaei N et al.**	RAC2 loss-of-function mutation in 2 siblings with characteristics of common variable immunodeficiency	2015	Journal of Allergy and Clinical Immunology 135(5): 1380-1384e1385 doi:10.1016/j.jaci.2014.10.039	1	0	
R15	**AlKhater SA**	CNS vasculitis and stroke as a complication of DOCK8 deficiency: A case report	2016	BMC Neurol 16(1): 54 doi:10.1186/s12883-016-0578-3	0	0	no fatality mentioned
R16	**Alsum Z, Al-Saud B et al.**	Disseminated cryptococcal infection in patient with novel JAK3 mutation severe combined immunodeficiency, with resolution after stem cell transplantation	2012	Pediatric Infectious Disease Journal 31(2): 204-206 doi:10.1097/INF.0b013e318239c3b3	0	0	no fatality mentioned
R17	**Alsum Z, Hawwari A et al.**	Clinical, immunological and molecular characterization of DOCK8 and DOCK8-like deficient patients: Single center experience of twenty five patients	2013	Journal of Clinical Immunology 33(1): 55-67 doi:10.1007/s10875-012-9769-x	5	0	(2 additional cases in list of cases with issues, one without clear gene candidate and one with unmentioned infectious agent for fatal pneumonia/sepsis)
R18	**Asgari S, McLaren PJ et al.**	Exome sequencing reveals primary immunodeficiencies in children with community-acquired Pseudomonas aeruginosa sepsis	2016	Frontiers in Immunology 7(SEP): ? doi:10.3389/fimmu.2016.00357	2	0	
R19	**Avila EM, Uzel G et al.**	Highly variable clinical phenotypes of hypomorphic RAG1 mutations	2010	Pediatrics 126(5): e1248-1252 doi:10.1542/peds.2009-3171	1	0	
R20	**Aviner S, Sofer D et al.**	Hemophagocytic lymphohistiocytosis associated with parechovirus 3 infection	2014	Journal of Pediatric Hematology/Oncology 36(4): e251-e253 doi:10.1097/MPH.0000000000000015	0	0	no fatality mentioned
R21	**Aydin SE, Kilic SS et al.**	DOCK8 Deficiency: Clinical and Immunological Phenotype and Treatment Options - a Review of 136 Patients	2015	Journal of Clinical Immunology 35(2): 189-198 doi:10.1007/s10875-014-0126-0	0	0	no individual patient data
R22	**Aytekin C, Dogu F et al.**	Purine nucleoside phosphorylase deficiency with fatal course in two sisters	2010	European Journal of Pediatrics 169(3): 311-314	2	0	
R23	**Baharin MF, Dhaliwal JS et al.**	A rare case of Wiskott-Aldrich Syndrome with normal platelet size: A case report	2016	Journal of Medical Case Reports 10(1): 188 doi:10.1186/s13256-016-0944-1	0	0	no fatality mentioned

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R24	**Baharin MF, Kader Ibrahim SB et al.**	Molecular characterization of two Malaysian patients with Wiskott-Aldrich syndrome	2015	Malaysian Journal of Pathology 37(2): 153-158	0	0	no infectious agent mentioned
R25	**Balci YI, Turul T et al.**	Hematopoietic stem cell transplantation from a donor with Klinefelter syndrome for Wiskott-Aldrich syndrome	2008	Pediatric Transplantation 12(5): 597-599 doi:10.1111/j.1399-3046.2008.00908.x	0	0	no fatality mentioned
R26	**Bandsma RH, van Goor H et al.**	Loss of ADAM17 is associated with severe multiorgan dysfunction	2015	Human Pathology 46(6): 923-928	2	0	
R27	**Banka S & Newman WG**	A clinical and molecular review of ubiquitous glucose-6-phosphatase deficiency caused by G6PC3 mutations	2013	Orphanet Journal Of Rare Diseases 8(1): 84 doi:10.1186/1750-1172-8-84	0	0	no infectious agent mentioned
R28	**Barmettler S, Nowak RJ et al.**	Previously undiagnosed fatal familial haemophagocytic lymphohistiocytosis in a 24-year-old woman	2016	BMJ Case Reports 2016(?): ? doi:10.1136/bcr-2015-213698	1	0	
R29	**Baumal CR, Levin AV & Read SE**	Cytomegalovirus retinitis in immunosuppressed children	1999	American Journal of Ophthalmology 127(5): 550-558	0	0	No genetical diagnosis, no clear gene candidate (2 more in list of cases with issues)
R30	**Beard LJ, Toogood IR et al.**	Early bone marrow transplantation in an infant with wiskott-aldrich syndrome	1991	Journal of Pediatric Hematology/Oncology 13(3): 310-314	0	0	no fatality: patient survived as can be concluded from abstract (no access to full text)
R31	**Beaussant Cohen S, Fenneteau O et al.**	Description and outcome of a cohort of 8 patients with WHIM syndrome from the French Severe Chronic Neutropenia Registry	2012	Orphanet Journal Of Rare Diseases 7(1): 71 doi:10.1186/1750-1172-7-71	2	0	
R32	**Bejaoui M, Barbouche MR et al.**	Primary immunodeficiency disorders in Tunisia: A study of 152 cases	1997	Archives de Pediatrie 4(9): 827-831 doi:10.1016/S0929-693X(97)88145-6	0	0	epidemiological data, no individual patient data
R33	**Bejaoui M, Mellouli F et al.**	The hyper-IgM syndrome: 13 Observations	2003	Presse Medicale 32(12): 544-549	0	0	no infectious agent identified
R34	**Ben-Farhat K, Ben-Mustapha I et al.**	A Founder Effect of c.257 + 2T > C Mutation in NCF2 Gene Underlies Severe Chronic Granulomatous Disease in Eleven Patients	2016	Journal of Clinical Immunology 36(6): 547-554 doi:10.1007/s10875-016-0299-9	2	0	
R35	**Ben-Khemis L, Mekki N et al.**	A founder mutation underlies a severe form of phosphoglutamase 3 (PGM3) deficiency in Tunisian patients	2017	Mol Immunol 90(?): 57-63 doi:10.1016/j.molimm.2017.06.248	0	0	no infectious agent mentioned
R36	**Berkel AI, Loos M et al.**	Clinical and immunological studies in a case of selective complete C1q deficiency	1979	Clinical and Experimental Immunology 38(1): 52-63	0	0	no infectious agent mentioned
R37	**Berkel AI, Petry F et al.**	Development of systemic lupus erythematosus in a patient with selective complete C1q deficiency	1997	European Journal of Pediatrics 156(2): 113-115 doi:10.1007/s004310050567	0	0	no infectious agent identified
R38	**Berthet F, Le Deist F et al.**	Clinical consequences and treatment of primary immunodeficiency syndromes characterized by functional T and B lymphocyte anomalies (combined immune deficiency)	1994	Pediatrics 93(2): 265-270	0	0	no clear gene candidates
R39	**Beser OF, Conde CD et al.**	Inflammatory Bowel Disease With Lethal Disease Course Caused by a Nonsense Mutation in BIRC4 Encoding X-Linked Inhibitor of Apoptosis Protein (XIAP)	2016	J Pediatr Gastroenterol Nutr 62(5): e41-43 doi:10.1097/mpg.0000000000000504	0	0	no infectious agent mentioned
R40	**Bhattacharya A, Slatter MA et al.**	Single centre experience of umbilical cord stem cell transplantation for primary immunodeficiency	2005	Bone Marrow Transplantation 36(4): 295-299 doi:10.1038/sj.bmt.1705054	1	0	
R41	**Binkley KE & Davis A, III et al.**	Clinical, biochemical, and genetic characterization of a novel estrogen-dependent inherited form of angioedema	2000	Journal of Allergy and Clinical Immunology 106(3): 546-550 doi:10.1067/mai.2000.108106	0	0	not PID
R42	**Blaydon DC, Biancheri P et al.**	Inflammatory skin and bowel disease linked to ADAM17 deletion	2011	New England Journal of Medicine 365(16): 1502-1508 doi:10.1056/NEJMoa1100721	0	1	(1 case cited by Bandsma 2015, mentioned sibling did not die)
R43	**Boggio E, Arico M et al.**	Mutation of FAS, XIAP, and UNC13D genes in a patient with a complex lymphoproliferative phenotype	2013	Pediatrics 132(4): e1052-1058	0	0	no infection, more likely autoimmune cause of death
R44	**Boisson B, Puel A et al.**	Human IκBα Gain of Function: a Severe and Syndromic Immunodeficiency	2017	Journal of Clinical Immunology 37(5): 397-412 doi:10.1007/s10875-017-0400-z	5	0	(1 additional case with questionable links between progressive tetraplegia and mentioned pathogens)
R45	**Bonney DK, O'Meara A et al.**	Successful allogeneic bone marrow transplant for Niemann-Pick disease type C2 is likely to be associated with a severe 'graft versus substrate' effect	2010	Journal of Inherited Metabolic Disease 33(SUPPL. 3): S171-S173 doi:10.1007/s10545-010-9060-3	0	0	no fatality mentioned
R46	**Booth C, Gilmour KC et al.**	X-linked lymphoproliferative disease due to SAP/SH2D1A deficiency: a multicenter study on the manifestations, management and outcome of the disease.	2011	Blood 117(1): 53-62	0	0	individual patient data on transplantation outcome does not include diagnosis, does not allow matching mentioned gene to patient
R47 §	**Boudghène-Stambouli O & Mérad-Boudia A**	Antifungal agents in dermatophytic disease: failure of griseofulvin, ketoconazole and itraconazole (In French)	1990	Bull Soc Pathol Exot 83(): 170-176	0	1	(1 single case cited by Lanternier 2013, no full text available)

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R48 §	**Boudghène-Stambouli O & Mérad-Boudia A**	Dermatophytic disease: exuberant hyperkeratosis with cutaneous horns	1998	Ann Dermatol Venereol 125(): 705–707	0	1	(1 single case cited by Lanternier 2013, no full text available)
R49	**Brambila-Tapia AJL, García-Ortiz JE et al.**	GATA2 null mutation associated with incomplete penetrance in a family with Emberger syndrome	2017	Hematology 22(8): 467-471 doi:10.1080/10245332.2017.1294551	0	0	no infectious agent mentioned
R50	**Brandau O, Schuster V et al.**	Epstein-Barr virus-negative boys with non-Hodgkin lymphoma are mutated in the SH2D1A gene, as are patients with X-linked lymphoproliferative disease (XLP)	1999	Human Molecular Genetics 8(13): 2407-2413 doi:10.1093/hmg/8.13.2407	2	0	(1 additional case without genetic diagnosis in list of cases with issues)
R51	**Breen C, Wynn RF et al.**	Developmental outcome post allogenic bone marrow transplant for Niemann Pick Type C2	2013	Molecular Genetics & Metabolism 108(1): 82-84	0	0	no fatality mentioned
R52	**Brochstein JA, Gillio AP et al.**	Marrow transplantation from human leukocyte antigen-identical or haploidentical donors for correction of Wiskott-Aldrich syndrome	1991	The Journal of pediatrics 119(6): 907-912 doi:10.1016/S0022-3476(05)83041-0	4	0	
R53	**Bryceson YT, Rudd E et al.**	Defective cytotoxic lymphocyte degranulation in syntaxin-11-deficient familial hemophagocytic lymphohistiocytosis 4 (FHL4) patients	2007	Blood 110(6): 1906-1915 doi:10.1182/blood-2007-02-074468	0	0	no patient data, cell biology study
R54	**Buchbinder D, Baker R et al.**	Identification of patients with RAG mutations previously diagnosed with common variable immunodeficiency disorders	2015	Journal of Clinical Immunology 35(2): 119-124	1	0	
R55	**Bukhari E, Alaklobi F et al.**	Disseminated bacille Calmette-Guérin disease in Saudi children: clinical profile, microbiology, immunology evaluation and outcome	2016	European Review for Medical and Pharmacological Sciences 20(17): 3696-3702	1	0	
R56	**Burda P, Kuster A et al.**	Characterization and review of MTHFD1 deficiency: four new patients, cellular delineation and response to folic and folinic acid treatment	2015	Journal of Inherited Metabolic Disease 38(5): 863-872	0	0	(1 fatal case with missing infectious agent in list of cases with issues)
R57	**Cabral-Marques O, Klaver S et al.**	First report of the hyper-IgM syndrome registry of the latin american society for immunodeficiencies: Novel mutations, unique infections, and outcomes	2014	Journal of Clinical Immunology 34(2): 146-156 doi:10.1007/s10875-013-9980-4	2	0	(2 additional cases with questionable link of infection with fatal event in list of cases with issues)
R58	**Caglayan Sozmen S, Isik S et al.**	Cyclosporin treatment improves skin findings in omenn syndrome	2015	Pediatric Dermatology 32(2): e54-57	0	0	no infectious agent specified
R59	**Canessa C, Romano F et al.**	Bcgitis and vaccine-derived poliovirus infection in a patient with a novel deletion in RAG1 binding site	2013	International Journal of Immunopathology & Pharmacology 26(2): 511-515 doi:10.1177/039463201302600225	0	0	no infectious agent mentioned
R60	**Cannioto Z, Berti I et al.**	IBD and IBD mimicking enterocolitis in children younger than 2 years of age	2009	European Journal of Pediatrics 168(2): 149-155 doi:10.1007/s00431-008-0721-2	1	0	
R61	**Capri Y, Vanlieferinghen P et al.**	Forme létale de syndrome de Netherton au sein d'une famille multiplex consanguine [A lethal variant of Netherton syndrome in a large inbred family]	2011	Archives de Pediatrie 18(3): 294-298 doi:10.1016/j.arcped.2010.12.005	0	0	should not have been excluded: fatal infection with unmentioned pathogens and invasive aspergillus with SPINK5 mutation.
R62	**Carlsson G, Fasth A et al.**	Incidence of severe congenital neutropenia in Sweden and risk of evolution to myelodysplastic syndrome/leukaemia	2012	British Journal of Haematology 158(3): 363-369 doi:10.1111/j.1365-2141.2012.09171.x	0	0	no infectious agent mentioned
R63	**Carvalho Neves Forte W, Ferreira De Carvalho Junior F et al.**	Evolution of IgA deficiency to IgG subclass deficiency and common variable immunodeficiency	2000	Allergologia et Immunopathologia 28(1): 18-20	0	0	no infectious agent mentioned, no genetic diagnosis
R64	**Casanova JL, Fieschi C et al.**	Revisiting human primary immunodeficiencies	2008	Journal of Internal Medicine 264(2): 115-127 doi:10.1111/j.1365-2796.2008.01971.x	0	0	no patients
R65	**Caselli D & Aricò M**	The role of BMT in childhood histiocytoses	2008	Bone Marrow Transplantation 41(SUPPL. 2): S8-S13 doi:10.1038/bmt.2008.46	0	0	no infectious agent mentioned
R66	**Cavkaytar O, Cagdas Ayvaz D et al.**	A case of DOCK8 deficient hyper-IgE syndrome presenting primarily with eczema, food allergy, and asthma	2013	Pediatric, Allergy, Immunology, and Pulmonology 26(1): 48-51 doi:10.1089/ped.2012.0179	1	0	
R67	**Cetica V, Santoro A et al.**	STXBP2 mutations in children with familial haemophagocytic lymphohistiocytosis type 5	2010	Journal of Medical Genetics 47(9): 595-600 doi:10.1136/jmg.2009.075341	0	0	no infectious agent mentioned
R68	**Chandesris MO, Melki I et al.**	Autosomal dominant STAT3 deficiency and hyper-IgE syndrome: Molecular, cellular, and clinical features from a french national survey	2012	Medicine (United States) 91(4): e1-e19 doi:10.1097/MD.0b013e31825f95b9	2	0	
R69	**Chapgier A, Kong XF et al.**	A partial form of recessive STAT1 deficiency in humans	2009	Journal of Clinical Investigation 119(6): 1502-1514 doi:10.1172/JCI37083	0	0	no fatality mentioned
R70	**Chen F, Li S et al.**	Clinical Heterogeneity of Interstitial Lung Disease in Polymyositis and Dermatomyositis Patients With or Without Specific Autoantibodies	2018	Am J Med Sci 355(1): 48-53 doi:10.1016/j.amjms.2017.07.013	0	0	no infectious agent mentioned, autoimmune disease
R71	**Chen N, Zhang ZY et al.**	The clinical features of autoimmunity in 53 patients with Wiskott–Aldrich syndrome in China: a single-center study	2015	European Journal of Pediatrics 174(10): 1311-1318 doi:10.1007/s00431-015-2527-3	0	0	no infectious agents mentioned in fatal cases

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R72	**Chen SH, Hsia SH et al.**	A possible familial lymphoproliferative disorder in two male siblings of children with recurrent wheezing and lung infections since infancy	2014	International Journal of Hematology 100(4): 407-412	0	0	mutational analysis did not find a responsible gene
R73	**Christmann M, Heitkamp S et al.**	Haemorrhagic cystitis and polyomavirus JC infection in ataxia telangiectasia	2009	Journal of pediatric urology 5(4): 324-326	0	0	Should not have been excluded: polyomavirus complications did only stop when corticosteroids were ceased, but interstitial lung disease worsened, leading to daeth.
R74	**Cicalese MP, Ferrua F et al.**	Update on the safety and efficacy of retroviral gene therapy for immunodeficiency due to adenosine deaminase deficiency.[Erratum appears in Blood. 2017 Jun 15;129(24):3271; PMID: 28620107]	2016	Blood 128(1): 45-54	0	0	no fatality mentioned
R75	**Clarke SLN, Bowron A et al.**	Barth syndrome	2013	Orphanet Journal Of Rare Diseases 8(1): 23 doi:10.1186/1750-1172-8-23	0	0	no individual patient data
R76	**Coffey AJ, Brooksbank RA et al.**	Host response to EBV infection in X-linked lymphoproliferative disease results from mutations in an SH2-domain encoding gene	1998	Nature Genetics 20(2): 129-135 doi:10.1038/2424	0	0	no individual cases
R77	**Colobran R, Alvarez de la Campa E et al.**	Clinical and structural impact of mutations affecting the residue Phe367 of FOXP3 in patients with IPEX syndrome	2016	Clinical Immunology 163(?): 60-65 doi:10.1016/j.clim.2015.12.014	1	0	
R78	**Cosson L, Toutain A et al.**	Barth syndrome in a female patient	2012	Molecular Genetics and Metabolism 106(1): 115-120 doi:10.1016/j.ymgme.2012.01.015	0	0	no infectious agent mentioned
R79 §	**Costa-Carvalho BT, De Moraes-Pinto MI et al.**	A remarkable depletion of both naive CD4+ and CD8+ with high proportion of memory T cells in an IPEX infant with a FOXP3 mutation in the forkhead domain	2008	Scand J Immunol 68(1): 85-91 doi:10.1111/j.1365-3083.2008.02055.x	0	1	(1 single case cited by Xavier-da-Silva 2015)
R80	**Cotto M, Cabanillas F et al.**	Epigenetic therapy of lymphoma using histone deacetylase inhibitors	2010	Clinical and Translational Oncology 12(6): 401-409 doi:10.1007/s12094-010-0527-3	0	0	not PID
R81	**Dalal I, Tabori U et al.**	Evolution of a T-B- SCID into an Omenn syndrome phenotype following parainfluenza 3 virus infection	2005	Clinical Immunology 115(1): 70-73 doi:10.1016/j.clim.2004.08.016	1	0	
R82	**Daschkey S, Bienemann K et al.**	Fatal Lymphoproliferative Disease in Two Siblings Lacking Functional FAAP24	2016	Journal of Clinical Immunology 36(7): 684-692	2	0	
R83	**De Greef JC, Wang J et al.**	Mutations in ZBTB24 are associated with immunodeficiency, centromeric instability, and facial anomalies syndrome type 2	2011	American Journal of Human Genetics 88(6): 796-804 doi:10.1016/j.ajhg.2011.04.018	2	0	
R84 §	**de la Calle-Martin O, Hernandez M et al.**	Familial CD8 deficiency due to a mutation in the CD8 alpha gene	2001	J Clin Invest. 2001 Jul(108(1)): 117-23 doi:10.1172/JCI10993	0	1	(1 single case cited by Mancebo 2008, family members only briefly mentioned)
R85	**De Luca F, Valenzise M et al.**	Sicilian family with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) and lethal lung disease in one of the affected brothers	2008	European Journal of Pediatrics 167(11): 1283-1288 doi:10.1007/s00431-008-0668-3	0	0	should not have been excluded: B. cepacia in APECED syndrome, associated with lung disease, confirmed AIRE mutation
R86	**de Souza TL, Fernandes RCSC et al.**	Microbial disease spectrum linked to a novel IL-12Rβ1 N-terminal signal peptide stop-gain homozygous mutation with paradoxical receptor cell-surface expression	2017	Frontiers in Microbiology 8(APR): ? doi:10.3389/fmicb.2017.00616	1	0	
R87	**Del Giudice E, Savoldi G et al.**	Acute inflammatory demyelinating polyradiculoneuropathy associated with perforin-deficient familial haemophagocytic lymphohistiocytosis	2003	Acta Paediatrica 92(3): 398-401	1	0	
R88	**Dhingra N, Yadav SP et al.**	Severe combined immunodeficiency caused by a new homozygous RAG1 mutation with progressive encephalopathy	2014	Hematology/oncology & stem cell therapy 7(1): 44-49 doi:10.1016/j.hemonc.2013.11.001	1	0	
R89	**Di WL, Mellerio JE et al.**	Phase i study protocol for Ex vivo lentiviral gene therapy for the inherited skin disease, netherton syndrome	2013	Human Gene Therapy Clinical Development 24(4): 182-190 doi:10.1089/humc.2013.195	0	0	study protocol (no results)
R90	**Dias C, McDonald A et al.**	Recurrent subacute post-viral onset of ataxia associated with a PRF1 mutation	2013	European Journal of Human Genetics 21(11): 1232-1239	0	0	should not have been excluded: varicella and PRF1
R91	**Díaz de Heredia C, Ortega JJ et al.**	Unrelated cord blood transplantation for severe combined immunodeficiency and other primary immunodeficiencies	2008	Bone Marrow Transplantation 41(7): 627-633 doi:10.1038/sj.bmt.1705946	0	0	individual patient data from various tables does not combine
R92	**Dimitrova D, Ong PY et al.**	Major Histocompatibility Complex Class II Deficiency Complicated by Mycobacterium avium Complex in a Boy of Mixed Ethnicity	2014	Journal of Clinical Immunology 34(6): 677-680 doi:10.1007/s10875-014-0048-x	0	0	no fatality mentioned
R93	**Diociaiuti A, Castiglia D et al.**	Lethal Netherton syndrome due to homozygous p.Arg371X mutation in SPINK5	2013	Pediatric Dermatology 30(4): e65-67	0	0	no infectious agent mentioned
R94	**Dobbs K, Dominguez Conde C et al.**	Inherited DOCK2 Deficiency in Patients with Early-Onset Invasive Infections	2015	New England Journal of Medicine 372(25): 2409-2422	2	0	
R95	**Döffinger R, Dupuis S et al.**	Inherited disorders of IL-12- and IFNγ-mediated immunity: A molecular genetics update	2002	Mol Immunol 38(12-13): 903-909 doi:10.1016/S0161-5890(02)00017-2	0	0	overview of mutations, no patient data

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R96	**Doncker AV, Balabanian K et al.**	Two cases of disseminated Mycobacterium avium infection associated with a new immunodeficiency syndrome related to CXCR4 dysfunctions	2011	Clinical Microbiology & Infection 17(2): 135-139 doi:10.1111/j.1469-0691.2010.03187.x	0	0	(1 additional case without clear genetic diagnosis in list of cases with issues)
R97	**Dupuis-Girod S, Medioni J et al.**	Autoimmunity in Wiskott-Aldrich syndrome: risk factors, clinical features, and outcome in a single-center cohort of 55 patients	2003	Pediatrics 111(5 Pt 1): e622-627	0	0	no individual patient data
R98	**Dutmer CM, Asturias EJ et al.**	Late Onset Hypomorphic RAG2 Deficiency Presentation with Fatal Vaccine-Strain VZV Infection	2015	Journal of Clinical Immunology 35(8): 754-760 doi:10.1007/s10875-015-0207-8	1	0	
R99 §	**Ege M, Ma Y et al.**	Omenn syndrome due to ARTEMIS mutations	2005	Blood 105(): 4179-4186 doi:10.1182/blood-2004-12-4861	0	1	(1 case cited by Lee 2013, two siblings mentioned with too little detail)
R100	**Ehlayel MS, Bener A & Laban MA**	Primary immunodeficiency diseases in children: 15 year experience in a tertiary care medical center in Qatar	2013	Journal of Clinical Immunology 33(2): 317-324 doi:10.1007/s10875-012-9812-y	0	0	epidemiological data, no individual cases
R101	**Ehmke N, Parvaneh N et al.**	First description of a patient with Vici syndrome due to a mutation affecting the penultimate exon of EPG5 and review of the literature	2014	American Journal of Medical Genetics, Part A 164(12): 3170-3175 doi:10.1002/ajmg.a.36772	0	0	no infectious agent mentioned
R102	**Eisen DP**	Mannose-binding lectin deficiency and respiratory tract infection	2010	J Innate Immun 2(2): 114-122 doi:10.1159/000228159	0	0	cell biology study
R103	**El-Maataoui O, Ailal F et al.**	Immunophenotyping of severe combined immunodeficiency in Morocco	2011	Immuno-Analyse et Biologie Specialisee 26(4): 161-164 doi:10.1016/j.immbio.2011.05.002	0	0	no individual patient data : epidemiologic data
R104	**Elkaim E, Neven B et al.**	Clinical and immunologic phenotype associated with activated phosphoinositide 3-kinase δ syndrome 2: A cohort study	2016	Journal of Allergy and Clinical Immunology 138(1): 210-218.e219 doi:10.1016/j.jaci.2016.03.022	1	0	
R105	**Enders A, Zieger B et al.**	Lethal hemophagocytic lymphohistiocytosis in Hermansky-Pudlak syndrome type II	2006	Blood 108(1): 81-87	1	0	
R106	**Erdos M, Garami M et al.**	Neuroendocrine carcinoma associated with X-linked hyper-immunoglobulin M syndrome: report of four cases and review of the literature	2008	Clinical Immunology 129(3): 455-461	0	0	should not have been excluded, various pathogens and CD40LG mutations
R107 §	**Etzioni A, Eidenschenk C et al.**	Fatal Varicella associated with selective natural killer cell deficiency	2005	J Pediatr 146(): 423-5 doi:10.1016/j.jpeds.2004.11.022	0	1	(1 single case cited by Hanna 2015)
R108	**Fabre A, Breton A et al.**	Syndromic (phenotypic) diarrhoea of infancy/tricho-hepato-enteric syndrome	2014	Archives of Disease in Childhood 99(1): 35-38 doi:10.1136/archdischild-2013-304016	0	0	no infectious agent mentioned
R109	**Faitelson Y, Bates A et al.**	A mutation in the STAT1 DNA-binding domain associated with hemophagocytic lymphohistocytosis	2014	LymphoSign Journal 1(2): 87-95 doi:10.14785/lpsn-2014-0004	0	0	1 case with questionable link of fatality and pathogens, in list of cases with issues.
R110	**Falkeis C, Mark W et al.**	Kidney transplantation in patients suffering from hereditary complete complement C4 deficiency	2007	Transplant International 20(12): 1044-1049 doi:10.1111/j.1432-2277.2007.00555.x	0	0	1 case of Kaposi's sarcoma and aspergillus pneumonia after kidney transplantation in C4A and C4B defect. Should not have been excluded.
R111	**Fazlollahi MR, Pourpak Z et al.**	Clinical, Laboratory, and Molecular Findings for 63 Patients With Severe Combined Immunodeficiency: A Decade s Experience	2017	J Investig Allergol Clin Immunol 27(5): 299-304 doi:10.18176/jiaci.0147	0	0	no individual patient data
R112	**Fellmann F, Angelini F et al.**	IL-17 receptor A and adenosine deaminase 2 deficiency in siblings with recurrent infections and chronic inflammation	2016	Journal of Allergy & Clinical Immunology 137(4): 1189-1196.e1182	1	0	
R113	**Filipovich AH, Shapiro RS et al.**	Unrelated donor bone marrow transplantation for correction of lethal congenital immunodeficiencies	1992	Blood 80(1): 270-276	0	0	no genetic diagnosis, but 1 patient with SCID did died of aspergillosis at day 20 post BMT
R114	**Fischer A, Landais P et al.**	Bone marrow transplantation (BMT) in Europe for primary immunodeficiencies other than severe combined immunodeficiency: a report from the European Group for BMT and the European Group for Immunodeficiency	1994	Blood 83(4): 1149-1154	0	0	cohort study with too little detail about individual cases
R115	**Folwaczny C, Ruelfs C et al.**	Ulcerative colitis in a patient with Wiskott-Aldrich syndrome	2002	Endoscopy 34(10): 840-841	1	0	
R116	**Foucar E, Rosai J et al.**	Immunologic abnormalities and their significance in sinus histiocytosis with massive lymphadenopathy	1984	American Journal of Clinical Pathology 82(5): 515-525 doi:10.1093/ajcp/82.5.515	0	0	no genetic diagnosis
R117	**Frigati LJ & Esser MM**	Chronic granulomatous disease and the challenges of diagnosis and management in South Africa	2016	Current Allergy and Clinical Immunology 29(2): 127-129	0	0	no fatality mentioned
R118	**Fuchs S, Rensing-Ehl A et al.**	Omenn syndrome associated with a functional reversion due to a somatic second-site mutation in CARD11 deficiency	2015	Blood 126(14): 1658-1669 doi:10.1182/blood-2015-03-631374	2	0	
R119	**Gámez-Díaz L, August D et al.**	The extended phenotype of LPS-responsive beige-like anchor protein (LRBA) deficiency	2016	Journal of Allergy and Clinical Immunology 137(1): 223-230 doi:10.1016/j.jaci.2015.09.025	0	0	no infectious agent mentioned

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R120	**Garcia-Laorden MI, Sole-Violan J et al.**	Mannose-binding lectin and mannose-binding lectin-associated serine protease 2 in susceptibility, severity, and outcome of pneumonia in adults	2008	Journal of Allergy and Clinical Immunology 122(2): 368-374.e362 doi:10.1016/j.jaci.2008.05.037	0	0	no individual patient data
R121	**Genel F, Ozbek E et al.**	Adenosine Deaminase-Deficient Severe Combined Immunodeficiency and Diffuse Large B-Cell Lymphoma	2015	Pediatric, Allergy, Immunology, and Pulmonology 28(2): 138-142 doi:10.1089/ped.2014.0478	0	0	no infectious agent mentioned
R122	**Gennery AR, Slatter MA et al.**	Hematopoietic stem cell transplantation corrects the immunologic abnormalities associated with immunodeficiency-centromeric instability-facial dysmorphism syndrome	2007	Pediatrics 120(5): e1341-e1344 doi:10.1542/peds.2007-0640	0	0	no fatality mentioned
R123	**Gerard LM, Barth D et al.**	Adult hemophagocytic lymphohistiocytosis with severe pulmonary hypertension and a novel perforin gene mutation	2012	International Journal of Hematology 95(4): 445-450 doi:10.1007/s12185-012-1029-6	0	0	1 case with complex causal chain of partly mentioned pathogens and HLH Is this a case of EBV- or HZV-triggered HLH?
R124	**Ghosh S, Schuster FR et al.**	Fatal outcome despite full lympho-hematopoietic reconstitution after allogeneic stem cell transplantation in atypical ataxia telangiectasia	2012	Journal of Clinical Immunology 32(3): 438-440 doi:10.1007/s10875-012-9654-7	0	0	cause of death is hepatic failure and encephalopathy.
R125	**Giannelou A, Wang H et al.**	Aberrant tRNA processing causes an autoinflammatory syndrome responsive to TNF inhibitors	2018	Ann Rheum Dis 77(4): 612-619 doi:10.1136/annrheumdis-2017-212401	1	0	
R126	**Glockel U, Schneider PM et al.**	Lethal pneumococcal meningitis in a one year old child with homozygous C2-deficiency	1990	Monatsschrift fur Kinderheilkunde 138(7): 399-402	1	0	
R127	**Gokce M, Tuncer M et al.**	Molecular diagnosis of Shwachman-diamond syndrome presenting with pancytopenia at an early age: The first report from Turkey	2013	Indian Journal of Hematology and Blood Transfusion 29(3): 161-163 doi:10.1007/s12288-012-0163-x	0	0	no infectious agent mentioned
R128	**Goldstein B, Khilnani P et al.**	Combined Immunodeficiency Associated with Xeroderma Pigmentosum	1990	Pediatric Dermatology 7(2): 132-135 doi:10.1111/j.1525-1470.1990.tb00669.x	0	0	not clear wchich PID gene may be involved. Xeroderma pigmentosum, died of Parainfluenza type 1.
R129	**Grace HJ, Brereton Stiles GG et al.**	A family with partial and total deficiency of complement C3	1976	South African Medical Journal 50(5): 139-140	1	0	
R130	**Grumach AS, Duarte AJS et al.**	Brazilian report on primary immunodeficiencies in children: 166 Cases studied over a follow-up time of 15 years	1997	Journal of Clinical Immunology 17(4): 340-345 doi:10.1023/A:1027335000994	0	0	Epidemiological data without individual data
R131	**Grunebaum E, Zhang J & Roifman CM**	Novel mutations and hot-spots in patients with purine nucleoside phosphorylase deficiency	2004	Nucleosides, Nucleotides and Nucleic Acids 23(8-9): 1411-1415 doi:10.1081/NCN-200027647	0	0	no cases
R132	**Guanà R, Garofalo S et al.**	The complex surgical management of the first case of severe combined immunodeficiency and multiple intestinal atresias surviving after the fourth year of life	2014	Pediatric Gastroenterology, Hepatology and Nutrition 17(4): 257-262 doi:10.5223/pghn.2014.17.4.257	0	0	no fatality mentioned
R133	**Guffroy A, Mourot-Cottet R et al.**	Neutropenia in Patients with Common Variable Immunodeficiency: a Rare Event Associated with Severe Outcome	2017	Journal of Clinical Immunology 37(7): 715-726 doi:10.1007/s10875-017-0434-2	0	0	no genetic diagnosis
R134	**Gunduz Z, Dursun I et al.**	A fatal Turkish case of CINCA-NOMID syndrome due to the novel Val-351-Leu CIAS1 gene mutation	2008	Rheumatology International 28(4): 379-383	0	0	no infectious agent mentioned
R135	**Gupta K, Rawat A et al.**	Infectious and non-infectious complications in primary immunodeficiency disorders: an autopsy study from North India	2018	J Clin Pathol 71(5): 425-435 doi:10.1136/jclinpath-2017-204708	3	0	(5 additional cases without (clear) genetic diagnosis in list of cases with issues)
R136	**Gurgey A, Unal S et al.**	Neonatal primary hemophagocytic lymphohistiocytosis in Turkish children	2008	Journal of Pediatric Hematology/Oncology 30(12): 871-876 doi:10.1097/MPH.0b013e31818a9577	0	0	only primary HLH, not triggered by infection
R137	**Haanpää M, Schlecht H et al.**	Interrupted/bipartite clavicle as a diagnostic clue in Kabuki syndrome	2017	American Journal of Medical Genetics, Part A 173(4): 1115-1118 doi:10.1002/ajmg.a.38131	0	0	1 abortion and one patient alive
R138	**Hacein-Bey Abina S, Gaspar HB et al.**	Outcomes following gene therapy in patients with severe Wiskott-Aldrich syndrome	2015	JAMA - Journal of the American Medical Association 313(15): 1550-1563 doi:10.1001/jama.2015.3253	1	0	
R139 §	**Hagleitner MM, Lankester A et al.**	Clinical spectrum of immunodeficiency, centromeric instability and facial dysmorphism (ICF syndrome)	2008	J Med Genet 45(2): 93-99 doi:10.1136/jmg.2007.053397	2	2	(2 cases cited by de Greef 2011) (1 additional case with questionable link between fatality and mentioned pathogen in list of cases with issues)
R140	**Halioui-Louhaichi S, Azzabi O et al.**	Primary immunodeficiencies: Report of 33 pediatric Tunisian cases	2016	Tunisie Medicale 94(4): 320-325	0	0	individual patient data from various tables cannot be combined
R141	**Hall MW, Gavrilin MA et al.**	Monocyte mRNA phenotype and adverse outcomes from pediatric multiple organ dysfunction syndrome	2007	Pediatric Research 62(5): 597-603 doi:10.1203/PDR.0b013e3181559774	0	0	no individual patient data
R142	**Halliday E, Winkelstein J & Webster ADB**	Enteroviral infections in primary immunodeficiency (PID): A survey of morbidity and mortality	2003	Journal of Infection 46(1): 1-8 doi:10.1053/jinf.2002.1066	0	0	no individual patient data
R143	**Hambleton S, Goodbourn S et al.**	STAT2 deficiency and susceptibility to viral illness in humans	2013	Proc Natl Acad Sci U S A 110(8): 3053-3058 doi:10.1073/pnas.1220098110	0	0	no infectious agent mentioned

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R144	**Hamidieh AA, Behfar M et al.**	Long-term outcomes of fludarabine, melphalan and antithymocyte globulin as reduced-intensity conditioning regimen for allogeneic hematopoietic stem cell transplantation in children with primary immunodeficiency disorders: a prospective single center study	2016	Bone Marrow Transplantation 51(2): 219-226	0	0	mentioned infectious complications cannot be matched to the listed patients
R145	**Han S, Koo HH et al.**	Common variation in genes related to immune response and risk of childhood leukemia	2012	Human Immunology 73(3): 316-319 doi:10.1016/j.humimm.2011.12.018	0	0	not PID
R146	**Hanna S, Béziat V et al.**	A homozygous mutation of RTEL1 in a child presenting with an apparently isolated natural killer cell deficiency	2015	Journal of Allergy and Clinical Immunology 136(4): 1113-1114 doi:10.1016/j.jaci.2015.04.021	1	0	
R147	**Hashii Y, Yoshida H et al.**	Hemophagocytosis after bone marrow transplantation for JAK3-deficient severe combined immunodeficiency	2010	Pediatric Transplantation 14(8): E105-109	0	0	no infectious agent mentioned
R148	**Hashimura Y, Nozu K et al.**	Minimal change nephrotic syndrome associated with immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome	2009	Pediatric Nephrology 24(6): 1181-1186 doi:10.1007/s00467-009-1119-8	0	0	no fatality mentioned
R149	**Hedayat M, Massaad MJ et al.**	Lessons in gene hunting: a RAG1 mutation presenting with agammaglobulinemia and absence of B cells	2014	Journal of Allergy & Clinical Immunology 134(4): 983-985.e981	0	0	no infectious agent mentioned
R150	**Heidelberger KP & LeGolvan DP**	Wiskott Aldrich syndrome and cerebral neoplasia: report of a case with localized reticulum cell sarcoma	1974	Cancer 33(1): 280-284 doi:10.1002/1097-0142(197401)33:1<280::AID-CNCR2820330141>3.0.CO;2-H	1	0	
R151	**Helminen M, Seitsonen S et al.**	A Novel Mutation W388X Underlying Properdin Deficiency in a Finnish Family	2012	Scandinavian Journal of Immunology 75(4): 445-448 doi:10.1111/j.1365-3083.2012.02674.x	0	0	no fatality mentioned
R152	**Heusele M, Clerson P et al.**	Risk factors for severe bacterial infections in patients with systemic autoimmune diseases receiving rituximab	2014	Clinical Rheumatology 33(6): 799-805 doi:10.1007/s10067-014-2509-2	0	0	not PID (induced by medication)
R153	**Horn J, Schlesier M et al.**	Fatal adult-onset antibody deficiency syndrome in a patient with cartilage hair hypoplasia	2010	Human Immunology 71(9): 916-919	1	0	
R154	**Horwich AL, Seashore MR & Dwyer JM**	Overwhelming Sepsis in the Adult Variant of Wiskott-Aldrich Syndrome	1984	Archives of Internal Medicine 144(7): 1498-1500 doi:10.1001/archinte.1984.00350190208036	1	0	
R155	**Huang KY, Lai MW et al.**	Fatal cytomegalovirus gastrointestinal disease in an infant with Wiskott-Aldrich syndrome	2008	Journal of the Formosan Medical Association 107(1): 64-67	1	0	
R156	**Huang KY, Shyur SD et al.**	Ataxia telangiectasia: report of two cases	2001	Journal of Microbiology, Immunology & Infection 34(1): 71-75	0	0	no infectious agent mentioned
R157	**Huang LH, Shyur SD et al.**	Disseminated Bacille Calmette-Guerin disease as the initial presentation of X-linked severe combined immunodeficiency--a case report	2005	Asian Pacific Journal of Allergy & Immunology 23(4): 221-226	0	0	duplicate publication without additional detail
R158	**Huang LH, Shyur SD et al.**	Disseminated cutaneous bacille Calmette-Guerin infection identified by polymerase chain reaction in a patient with X-linked severe combined immunodeficiency	2006	Pediatric Dermatology 23(6): 560-563	1	0	
R159	**Hügle B, Suchowerskyj P et al.**	Persistent Hypogammaglobulinemia Following Mononucleosis in Boys Is Highly Suggestive of X-Linked Lymphoproliferative Disease - Report of Three Cases	2004	Journal of Clinical Immunology 24(5): 515-522 doi:10.1023/B:JOCI.0000040922.26286.36	0	0	no fatality mentioned
R160	**Huppmann AR, Leiding JW et al.**	Pathologic findings in NEMO deficiency: A surgical and autopsy survey	2015	Pediatric and Developmental Pathology 18(5): 387-400 doi:10.2350/15-05-1631-OA.1	5	0	(1 additional case with questionable link between fatality and mentioned infectious agents)
R161	**Ilowite NT, Fligner CL & Ochs HD**	Pulmonary angiitis with atypical lymphoreticular infiltrates in Wiskott-Aldrich syndrome: Possible relationship of lymphomatoid granulomatosis and EBV infection	1986	Clinical Immunology and Immunopathology 41(3): 479-484 doi:10.1016/0090-1229(86)90018-8	1	0	
R162	**Imai K, Morio T et al.**	Clinical course of patients with WASP gene mutations	2004	Blood 103(2): 456-464 doi:10.1182/blood-2003-05-1480	0	0	not clear which 2 patients died of infection: 1 patient died of JC virus encephalitis after bone marrow transplantation, 1 patient died of EBV-associated B-cell lymphoma, author may be able to tell, E-mail sent.
R163	**Isman-Nelkenbaum G, Wolach B et al.**	Chronic granulomatous disease of childhood: An unusual cause of recurrent uncommon infections in a 61-year-old man	2011	Clinical and Experimental Dermatology 36(7): 759-762 doi:10.1111/j.1365-2230.2011.04101.x	0	0	no fatality mentioned
R164	**Iwatani S, Uemura K et al.**	Familial Hemophagocytic Lymphohistiocytosis Presenting as Hydrops Fetalis	2014	AJP Reports 5(1): e22-e24 doi:10.1055/s-0034-1544110	1	0	
R165	**Jennane S, El Kababri M et al.**	Un syndrome d'activation macrophagique révélant un syndrome de Griscelli de type 2 [A hemophagocytic syndrome revealing a Griscelli syndrome type 2]	2013	Annales de Biologie Clinique 71(4): 461-464	0	0	no infectious agent identified

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R166	**Jin YY, Zhou W et al.**	Variable clinical phenotypes of X-linked lymphoproliferative syndrome in China: Report of five cases with three novel mutations and review of the literature	2016	Human Immunology 77(8): 658-666 doi:10.1016/j.humimm.2016.06.005	0	0	no infectious agents mentioned
R167	**Jing H, Zhang Q et al.**	Somatic reversion in dedicator of cytokinesis 8 immunodeficiency modulates disease phenotype	2014	Journal of Allergy and Clinical Immunology 133(6): 1667-1675 doi:10.1016/j.jaci.2014.03.025	0	0	no individual patient data
R168	**Jönsson G, Truedsson L et al.**	Hereditary C2 deficiency in Sweden: Frequent occurrence of invasive infection, atherosclerosis, and rheumatic disease	2005	Medicine 84(1): 23-34 doi:10.1097/01.md.0000152371.22747.1e	3	0	
R169	**Jouanguy E, Lamhamedi-Cherradi S et al.**	Partial interferon-γ receptor 1 deficiency in a child with tuberculoid bacillus Calmette-Guerin infection and a sibling with clinical tuberculosis	1997	Journal of Clinical Investigation 100(11): 2658-2664	0	0	no fatality mentioned
R170	**Kalman L, Lindegren ML et al.**	Mutations in genes required for T-cell development: IL7R, CD45, IL2RG, JAK3, IMG1, IMG2, ARTEMIS, and ADA and severe combined immunodeficiency: HuGE review	2004	Genetics in Medicine 6(1): 16-26 doi:10.1097/01.GIM.0000105752.80592.A3	0	0	no individual patient data
R171	**Kanegane H, Ito Y et al.**	X-linked lymphoproliferative syndrome presenting with systemic lymphocytic vasculitis	2005	American Journal of Hematology 78(2): 130-133 doi:10.1002/ajh.20261	0	0	no fatality mentioned
R172	**Kanegane H, Taneichi H et al.**	Severe neutropenia in Japanese patients with X-linked agammaglobulinemia	2005	Journal of Clinical Immunology 25(5): 491-495 doi:10.1007/s10875-005-5370-x	2	0	
R173	**Kaufman DA, Hershfield MS et al.**	Cerebral lymphoma in an adenosine deaminase-deficient patient with severe combined immunodeficiency receiving polyethylene glycol-conjugated adenosine deaminase	2005	Pediatrics 116(6): e876-879	0	0	no infectious agent mentioned apart from uneventful varicella years earlier
R174	**Kaya Z, Bay A et al.**	Prognostic Factors and Long-Term Outcome in 52 Turkish Children With Hemophagocytic Lymphohistiocytosis	2015	Pediatric Critical Care Medicine 16(6): e165-173 doi:10.1097/PCC.0000000000000449	0	0	no individual patient data
R175	**Kaya Z, Ehl S et al.**	A novel single point mutation of the LYST gene in two siblings with different phenotypic features of Chediak Higashi syndrome	2011	Pediatric Blood & Cancer 56(7): 1136-1139 doi:10.1002/pbc.22878	1	0	
R176	**Keiser PB & Broderick M**	Meningococcal polysaccharide vaccine failure in a patient with C7 deficiency and a decreased anti-capsular antibody response	2012	Human vaccines & Immunotherapeutics 8(5): 582-586 doi:10.4161/hv.19517	0	0	no infectious agent identified
R177	**Kersey JH, Shapiro RS & Filipovich AH**	Relationship of immunodeficiency to lymphoid malignancy	1988	Pediatric Infectious Disease Journal 7(5): S10-S12	0	0	no patient data, textbook style
R178	**Khalilzadeh S, Boloorsaz MR et al.**	Primary immunodeficiency in children: Report of seven years study	2011	Tanaffos 10(2): 38-43	0	0	no individual patient data
R179	**Khan TA, Iqbal A et al.**	Novel RAG1 mutation and the occurrence of mycobacterial and Chromobacterium violaceum infections in a case of leaky SCID	2017	Microb Pathog 109(?): 114-119 doi:10.1016/j.micpath.2017.05.033	0	0	1 fatal case with unmentioned pathogens post-HSCT in list of cases with issues.
R180	**Kilic SS, van Wengen A et al.**	Severe disseminated mycobacterial infection in a boy with a novel mutation leading to IFN-gammaR2 deficiency	2012	Journal of Infection 65(6): 568-572 doi:10.1016/j.jinf.2012.08.008	1	0	
R181	**Kim HJ, Song MJ et al.**	Paternal Somatic Mosaicism of a Novel Frameshift Mutation in ELANE Causing Severe Congenital Neutropenia	2015	Pediatric Blood and Cancer 62(12): 2229-2231 doi:10.1002/pbc.25654	0	0	no fatality mentioned
R182	**Kim HY, Kim YM & Park HJ**	Disseminated BCG pneumonitis revealing severe combined immunodeficiencyxs in CHARGE syndrome	2017	Pediatric Pulmonology 52(2): E4-E6	0	0	(1 case without genetic diagnosis in list of cases with issues)
R183	**Kim JY, Shin JH et al.**	A novel PRF1 gene mutation in a fatal neonate case with type 2 familial hemophagocytic lymphohistiocytosis	2014	Korean Journal of Pediatrics 57(1): 50-53 doi:10.3345/kjp.2014.57.1.50	0	0	no infectious agent identified
R184	**Kinnear C, Glanzmann B et al.**	Exome sequencing identifies a novel TTC37 mutation in the first reported case of Trichohepatoenteric syndrome (THE-S) in South Africa	2017	BMC Medical Genetics 18(1): 26	2	0	
R185	**Klupp N, Simonitsch I et al.**	Emergence of an unusual bone marrow precursor B-cell population in fatal Shwachman-Diamond syndrome	2000	Archives of Pathology & Laboratory Medicine 124(9): 1379-1381 doi:10.1043/0003-9985(2000)124<1379:EOAUBM>2.0.CO;2	0	0	no infectious agent mentioned
R186	**Knoblauch H, Tennstedt C et al.**	Two brothers with findings resembling congenital intrauterine infection-like syndrome (Pseudo-TORCH syndrome)	2003	American Journal of Medical Genetics 120 A(2): 261-265	0	0	not PID
R187	**Koker MY, Camcioglu Y et al.**	Clinical, functional, and genetic characterization of chronic granulomatous disease in 89 Turkish patients	2013	Journal of Allergy & Clinical Immunology 132(5): 1156-1163.e1155	0	0	no individual patient data
R188	**Kondoh T, Matsumoto T & Tsuji Y**	Wiskott-aldrich syndrome in two sisters	1997	Japanese Journal of Human Genetics 42(1): 78	0	0	no infection

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R189	**Koo S, Kejariwal D et al.**	Oesophageal candidiasis and squamous cell cancer in patients with gain-of-function STAT1 gene mutation	2017	United European Gastroenterology Journal 5(5): 625-631 doi:10.1177/2050640616684404	0	0	case series with examples of CMC leading to cancer and eventually death with STAT1 AD mutations. Should not have been excluded
R190	**Kostel Bal S, Haskologlu S et al.**	Multiple Presentations of LRBA Deficiency: a Single-Center Experience	2017	J Clin Immunol 37(8): 790-800 doi:10.1007/s10875-017-0446-y	1	0	(1 additional case with unclear role of pathogens in list of cases with issues)
R191	**Kropski JA, Mitchell DB et al.**	A novel dyskerin (DKC1) mutation is associated with familial interstitial pneumonia	2014	Chest 146(1): e1-e7 doi:10.1378/chest.13-2224	0	0	not PID, no fatality mentioned
R192	**Krutikhina SB, Gorelov AV et al.**	Study of periodic disease in children under the conditions of a large megapolis	2016	New Armenian Medical Journal 10(4): 28-33	0	0	not PID
R193	**Kuhns DB, Fink DL et al.**	Cytoskeletal abnormalities and neutrophil dysfunction in WDR1 deficiency	2016	Blood 128(17): 2135-2143 doi:10.1182/blood-2016-03-706028	1	0	
R194	**Kuijpers TW, Alders M et al.**	Hematologic abnormalities in Shwachman Diamond syndrome: Lack of genotype-phenotype relationship	2005	Blood 106(1): 356-361 doi:10.1182/blood-2004-11-4371	0	0	no fatality mentioned
R195	**Kulkarni M, Desai M et al.**	Clinical, Immunological, and Molecular Findings of Patients with p47phox Defect Chronic Granulomatous Disease (CGD) in Indian Families	2016	Journal of Clinical Immunology 36(8): 774-784 doi:10.1007/s10875-016-0333-y	0	0	no individual patient data
R196	**Kusuhara K, Yamamoto K et al.**	Association of IL12RB1 polymorphisms with susceptibility to and severity of tuberculosis in Japanese: A gene-based association analysis of 21 candidate genes	2007	International Journal of Immunogenetics 34(1): 35-44 doi:10.1111/j.1744-313X.2007.00653.x	0	0	not PID
R197	**Lainka E, Hershfield MS et al.**	Polyethylene glycol-conjugated adenosine deaminase (ADA) therapy provides temporary immune reconstitution to a child with delayed-onset ADA deficiency	2005	Clinical and Diagnostic Laboratory Immunology 12(7): 861-866 doi:10.1128/CDLI.12.7.861-866.2005	0	0	(1 case without infectious agent in list of cases with issues)
R198	**Lanternier F, Barbati E et al.**	Inherited CARD9 deficiency in 2 unrelated patients with invasive exophiala infection	2015	Journal of Infectious Diseases 211(8): 1241-1250 doi:10.1093/infdis/jiu412	0	0	did not die (supplementary data)
R199	**Lanternier F, Pathan S et al.**	Deep dermatophytosis and inherited CARD9 deficiency	2013	New England Journal of Medicine 369(18): 1704-1714 doi:10.1056/NEJMoa1208487	4	0	
R200	**Lebel A, Yacobovich J et al.**	Genetic analysis and clinical picture of severe congenital neutropenia in Israel	2015	Pediatric Blood & Cancer 62(1): 103-108 doi:10.1002/pbc.25251	0	0	no infectious agent mentioned
R201	**Lee KH, Shyur SD et al.**	Clinical manifestations and BTK gene defect in 4 unrelated Taiwanese families with Bruton's disease	2011	Asian Pacific Journal of Allergy and Immunology 29(3): 260-265	1	0	
R202	**Lee PP, Woodbine L et al.**	The many faces of Artemis-deficient combined immunodeficiency - Two patients with DCLRE1C mutations and a systematic literature review of genotype-phenotype correlation	2013	Clinical Immunology 149(PB): 464-474 doi:10.1016/j.clim.2013.08.006	6	0	(1 additional case with transplant-related complications not further specified in list of cases with issues)
R203	**Lee WI, Chen CC et al.**	A Nationwide Study of Severe and Protracted Diarrhoea in Patients with Primary Immunodeficiency Diseases	2017	Sci Rep 7(1): 3669 doi:10.1038/s41598-017-03967-4	5	0	
R204	**Lee WI, Chen SH et al.**	Clinical aspects, immunologic assessment, and genetic analysis in taiwanese children with hemophagocytic lymphohistiocytosis	2009	Pediatric Infectious Disease Journal 28(1): 30-34 doi:10.1097/INF.0b013e3181813592	0	0	no individual patient data
R205	**Lee WI, Huang JL et al.**	Clinical aspects and genetic analysis of taiwanese patients with wiskott-Aldrich syndrome protein mutation: the first identification of x-linked thrombocytopenia in the chinese with novel mutations	2010	Journal of Clinical Immunology 30(4): 593-601	4	0	
R206	**Lee WI, Huang JL, Jaing TH et al.**	Distribution, clinical features and treatment in Taiwanese patients with symptomatic primary immunodeficiency diseases (PIDs) in a nationwide population-based study during 1985-2010	2011	Immunobiology 216(12): 1286-1294 doi:10.1016/j.imbio.2011.06.002	0	0	no individual patient data
R207	**Lee WI, Huang JL, Lin SJ et al.**	Clinical, immunological and genetic features in Taiwanese patients with the phenotype of hyper-immunoglobulin E recurrent infection syndromes (HIES)	2011	Immunobiology 216(8): 909-917 doi:10.1016/j.imbio.2011.01.008	0	0	(2 cases without genetic diagnosis in list of cases with issues)
R208	**Lee WI, Huang JL et al.**	Clinical features and genetic analysis of Taiwanese patients with the hyper IgM syndrome phenotype	2013	Pediatric Infectious Disease Journal 32(9): 1010-1016 doi:10.1097/INF.0b013e3182936280	1	0	(1 additional case with questionable link of fatality with mentioned infectious agent)
R209	**Lee WI, Huang JL, Chen CC et al.**	Identifying mutations of the tetratricopeptide repeat domain 37 (TTC37) gene in infants with intractable diarrhea and a comparison of asian and non-asian phenotype and genotype: A global case-report study of a well-defined syndrome with immunodeficiency	2016	Medicine (United States) 95(9): e2918 doi:10.1097/MD.0000000000002918	1	0	
R210	**Lee WI, Huang JL, Yeh KW et al.**	The effects of prenatal genetic analysis on fetuses born to carrier mothers with primary immunodeficiency diseases	2016	Annals of Medicine 48(1-2): 103-110 doi:10.3109/07853890.2016.1140224	0	0	should not have been excluded… 4 eligible cases

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R211	**Lee WI, Kuo ML et al.**	Distribution and clinical aspects of primary immunodeficiencies in a Taiwan pediatric tertiary hospital during a 20-year period	2005	Journal of Clinical Immunology 25(2): 162-173 doi:10.1007/s10875-005-2822-2	2	0	
R212	**Leitão MF, Vilela MMS et al.**	Complement factor I deficiency in a family with recurrent infections	1997	Immunopharmacology 38(1-2): 207-213 doi:10.1016/S0162-3109(97)00080-5	0	0	no infectious agent mentioned
R213	**Leven EA, Maffucci P et al.**	Hyper IgM Syndrome: a Report from the USIDNET Registry	2016	Journal of Clinical Immunology 36(5): 490-501 doi:10.1007/s10875-016-0291-4	0	0	13 of 84 patients died, 5 infectious causes, but not enough individual patient data. 83 of 84 patients have a mutation in CD40LG and 1 AICDA. Should maybe not have been excluded…
R214	**Levy J, Espanol-Boren T et al.**	Clinical spectrum of X-linked hyper-IgM syndrome	1997	Journal of Pediatrics 131(1 Pt 1): 47-54	0	0	no individual patient data
R215 §	**Levy-Lahad E & Wildin RS**	Neonatal diabetes mellitus, enteropathy, thrombocytopenia, and endocrinopathy: Further evidence for an X-linked lethal syndromeNeonatal diabetes mellitus, enteropathy, thrombocytopenia, and endocrinopathy: Further evidence for an X-linked lethal syndrome	2001	J Pediatr 138(4): 577-80 doi:10.1067/mpd.2001.111502	0	1	(1 case cited by Xavier-da-Silva 2015, the other two were dismissed for lack of detail on pathogens)
R216	**Lewandowski K, Zozulińska M et al.**	Normal sialophorine (CD43) expression in a thrombocytopenic and immunodeficient woman carrier of Wiskott-Aldrich syndrome	1996	Clinical and Applied Thrombosis/Hemostasis 2(2): 137-141 doi:10.1177/107602969600200209	0	0	index patient survived, family history not detailed enough for inclusion of deceased siblings
R217	**Li FY, Chaigne-Delalande B et al.**	XMEN disease: A new primary immunodeficiency affecting Mg2+ regulation of immunity against Epstein-Barr virus	2014	Blood 123(14): 2148-2152 doi:10.1182/blood-2013-11-538686	2	0	
R218	**Lima Filho ADB, Carmo R et al.**	Complement and mannose-binding lectin 2 polymorphism in Meningococcal disease	2012	Clinical Laboratory 58(11-12): 1165-1169 doi:10.7754/Clin.Lab.2012.111119	0	0	no individual patient data
R219	**Lin JH, Yu-Yun Lee J et al.**	DKC1 gene mutation in a Taiwanese kindred with X-linked dyskeratosis congenita	2002	Kaohsiung Journal of Medical Sciences 18(11): 573-577	1	0	
R220	**Lin SC, Shyur SD et al.**	X-linked hyper-immunoglobulin M syndrome: Molecular genetic study and long-time follow-up of three generations of a Chinese family	2006	International Archives of Allergy and Immunology 140(1): 1-8 doi:10.1159/000091744	0	0	no infectious agent mentioned
R221	**Linden MG, Bender BG & Robinson A**	C7 complement deficiency in an Israeli Arab village	2002	American Journal of Medical Genetics 110(1): 25-29 doi:10.1002/ajmg.10393	0	0	no fatalities mentioned
R222	**Litzman J, Jones A et al.**	Intravenous immunoglobulin, splenectomy, and antibiotic prophylaxis in Wiskott-Aldrich syndrome	1996	Archives of Disease in Childhood 75(5): 436-439 doi:10.1136/adc.75.5.436	0	0	no individual patient data
R223	**Liu QF, Fan ZP et al.**	Epstein-Barr virus-associated pneumonia in patients with post-transplant lymphoproliferative disease after hematopoietic stem cell transplantation	2010	Transplant Infectious Disease 12(4): 284-291 doi:10.1111/j.1399-3062.2010.00502.x	0	0	not PID
R224	**Liu X, Zhou K et al.**	A delayed diagnosis of X-linked hyper IgM syndrome complicated with toxoplasmic encephalitis in a child: A case report and literature review	2017	Medicine (United States) 96(49): e8989 doi:10.1097/MD.0000000000008989	2	0	
R225	**Lord JD, Chen J & Kozarek RA**	A case of fatal idiopathic enteritis and multiple opportunistic infections associated with dendritic cell deficiencies	2013	Journal of Gastrointestinal & Liver Diseases 22(1): 87-91	0	0	no gene candidate, not infection
R226	**Lu G & Yu D**	Case report of X-linked hyper-IgM syndrome with acquired toxoplasmic encephalitis	2017	Genetics and Molecular Research 16(4): ? doi:10.4238/gmr16039822	1	0	
R227	**Lugo Reyes SO, Ramirez-Vazquez G et al.**	Clinical Features, Non-Infectious Manifestations and Survival Analysis of 161 Children with Primary Immunodeficiency in Mexico: A Single Center Experience Over two Decades	2016	Journal of Clinical Immunology 36(1): 56-65 doi:10.1007/s10875-015-0226-5	0	0	no individual patient data
R228	**Lundin KE, Hamasy A et al.**	Susceptibility to infections, without concomitant hyper-IgE, reported in 1976, is caused by hypomorphic mutation in the phosphoglucomutase 3 (PGM3) gene	2015	Clinical Immunology 161(2): 366-372 doi:10.1016/j.clim.2015.10.002	1	0	
R229	**Lynch MK, Jones CH et al.**	Necrotizing enterocolitis in an infant with Omenn syndrome	2006	Allergy and Asthma Proceedings 27(6): 537-543 doi:10.2500/aap.2006.27.2893	1	0	
R230	**Mak CM, Lam CW et al.**	Fatal viral infection-associated encephalopathy in two Chinese boys: a genetically determined risk factor of thermolabile carnitine palmitoyltransferase II variants	2011	Journal of Human Genetics 56(8): 617-621	0	0	not PID
R231	**Malkan UY, Gunes G et al.**	Common variable immune deficiency associated hodgkin's lymphoma complicated with EBV-linked hemophagocytic lymphohistiocytosis: A case report	2015	International Journal of Clinical and Experimental Medicine 8(8): 14203-14206	0	0	no infection
R232	**Mamlok RJ, Mamlok V et al.**	Glucose-6-phosphate dehydrogenase deficiency, neutrophil dysfunction and Chromobacterium violaceum sepsis	1987	Journal of Pediatrics 111(6 I): 852-854 doi:10.1016/S0022-3476(87)80203-2	0	0	should not have been excluded: G6PD and C. violaceum.

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R233	**Mancebo E, Moreno-Pelayo MA et al.**	Gly111Ser mutation in CD8A gene causing CD8 immunodeficiency is found in Spanish Gypsies	2008	Mol Immunol 45(2): 479-484 doi:10.1016/j.molimm.2007.05.022	1	0	
R234	**Mansour S, Woffendin H et al.**	Incontinentia pigmenti in a surviving male is accompanied by hypohidrotic ectodermal dysplasia and recurrent infection	2001	American Journal of Medical Genetics 99(2): 172-177 doi:10.1002/1096-8628(2001)9999:9999<::AID-AJMG1155>3.0.CO;2-Y	1	0	
R235	**Marco EJ, Anderson JE et al.**	Acute necrotizing encephalopathy in 3 brothers	2010	Pediatrics 125(3): e693-698 doi:10.1542/peds.2009-1984	0	0	not PID
R236	**Marcus N**	Immunodeficiency and severe gastrointestinal manifestations in a patient with novel DKC1 mutations causing Hoyeraal-Hreidarsson syndrome	2016	LymphoSign Journal 3(3): 119-126 doi:10.14785/lymphosign-2016-0006	0	0	no infectious agent identified
R237	**Marquart HV, Schejbel L et al.**	C1q deficiency in an Inuit family: Identification of a new class of C1q disease-causing mutations	2007	Clinical Immunology 124(1): 33-40 doi:10.1016/j.clim.2007.03.547	1	0	
R238	**Martinez-Martinez L, Vazquez-Ortiz M et al.**	From Severe Combined Immunodeficiency to Omenn syndrome after hematopoietic stem cell transplantation in a RAG1 deficient family	2012	Pediatric Allergy & Immunology 23(7): 660-666 doi:10.1111/j.1399-3038.2012.01339.x	2	0	
R239	**Masri A, Bakri FG et al.**	Griscelli syndrome type 2: a rare and lethal disorder	2008	Journal of Child Neurology 23(8): 964-967	0	0	no fatality mentioned
R240	**Mathieu AL, Verronese E et al.**	PRKDC mutations associated with immunodeficiency, granuloma, and autoimmune regulator-dependent autoimmunity	2015	Journal of Allergy and Clinical Immunology 135(6): 1578-1588 doi:10.1016/j.jaci.2015.01.040	0	0	no fatality mentioned
R241	**McCarty GA & Synderman R**	Component deficiencies. 5. The fifth component	1986	Progress in Allergy 39(?): 271-282	0	0	no infectious fatalities
R242	**Meschede IP, Santos TO et al.**	Griscelli syndrome-type 2 in twin siblings: case report and update on RAB27A human mutations and gene structure	2008	Brazilian Journal of Medical & Biological Research 41(10): 839-848	0	0	
R243	**Minocha P, Choudhary R et al.**	Griscelli syndrome subtype 2 with hemophagocytic lympho-histiocytosis: A case report and review of literature	2017	Intractable and Rare Diseases Research 6(1): 76-79 doi:10.5582/irdr.2016.01084	0	0	no fatality mentioned
R244	**Mitsui-Sekinaka K, Imai K et al.**	Clinical features and hematopoietic stem cell transplantations for CD40 ligand deficiency in Japan	2015	Journal of Allergy and Clinical Immunology 136(4): 1018-1024 doi:10.1016/j.jaci.2015.02.020	0	0	no individual patient data
R245	**Mohammadinejad P, Pourhamdi S et al.**	Primary antibody deficiency in a tertiary referral hospital: A 30-year experiment	2015	Journal of Investigational Allergology and Clinical Immunology 25(6): 416-425	0	0	no individual patient data
R246	**Möller M, Nebel A et al.**	Host susceptibility to tuberculosis: CARD15 polymorphisms in a South African population	2007	Molecular and Cellular Probes 21(2): 148-151 doi:10.1016/j.mcp.2006.10.001	0	0	study concludes that CARD19 is not a major susceptibility gene for TB in dark skinned people in South Africa. Should maybe not have been excluded?
R247	**Moller Rasmussen J, Teisner B et al.**	Three cases of factor I deficiency: The effect of treatment with plasma	1988	Clinical and Experimental Immunology 74(1): 131-136	0	0	1 of 3 cases mentioned a fatality due to polyarteritis nodosa, no infectious agent mentioned for this case.
R248	**Moncada-Velez M, Velez-Ortega A et al.**	Somatic mosaicism caused by monoallelic reversion of a mutation in T cells of a patient with ADA-SCID and the effects of enzyme replacement therapy on the revertant phenotype	2011	Scandinavian Journal of Immunology 74(5): 471-481	0	0	no infectious agent mentioned
R249	**Monga A, Makkar RPS et al.**	Case report: Acute hepatitis E infection with coexistent glucose-6-phosphate dehydrogenase deficiency	2003	Canadian Journal of Infectious Diseases 14(4): 230-231 doi:10.1155/2003/913679	0	0	should not have been excluded: G6PD with HEV fatality
R250	**Morales M, Bakshi S et al.**	SCID variants with unusual immunologic presentation	1998	FASEB Journal 12(5): A893-A893	2	0	
R251 §	**Moriya K, Sasahara Y et al.**	IKBA S32 Mutations Underlie Ectodermal Dysplasia with Immunodeficiency and Severe Noninfectious Systemic Inflammation	2018	Journal of Clinical Immunology 38(): 543–545 doi:10.1007/s10875-018-0522-y	0	2	(same cases as Boisson 2017, mentioned in personal communication Bertrand Boisson)
R252	**Morra M, Silander O et al.**	Alterations of the X-linked lymphoproliferative disease gene SH2D1A in common variable immunodeficiency syndrome	2001	Blood 98(5): 1321-1325 doi:10.1182/blood.V98.5.1321	2	0	
R253	**Mortaz E, Marashian SM et al.**	A new ataxia-telangiectasia mutation in an 11-year-old female	2017	Immunogenetics 69(7): 415-419 doi:10.1007/s00251-017-0983-9	1	0	
R254 §	**Moshous D, Pannetier C et al.**	Partial T and B lymphocyte immunodeficiency and predisposition to lymphoma in patients with hypomorphic mutations in Artemis	2003	J. Clin. Invest. 111(3): 381-387 doi:10.1172/JCI16774	0	4	(all 4 cases cited by Lee 2013)
R255	**Moya-Quiles MR, Bernardo-Pisa MV et al.**	Severe combined immunodeficiency: First report of a de novo mutation in the IL2RG gene in a boy conceived by in vitro fertilization	2014	Clinical Genetics 85(5): 500-501 doi:10.1111/cge.12208	1	0	

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R256	**Muschke P, Gola H et al.**	Retrospective diagnosis and subsequent prenatal diagnosis of Nijmegen breakage syndrome	2004	Prenatal Diagnosis 24(2): 111-113	0	0	no infectious agent mentioned
R257	**My LT, Lien LB et al.**	Comprehensive analyses and characterization of haemophagocytic lymphohistiocytosis in Vietnamese children	2010	British Journal of Haematology 148(2): 301-310 doi:10.1111/j.1365-2141.2009.07957.x	0	0	no individual patient data
R258 §	**Myers AK, Perroni L et al.**	Clinical and molecular findings in IPEX syndrome	2006	Arch Dis Child 91(1): 63-4 doi:10.1136/adc.2005.078287	1	1	(1 case cited by Xavier-da-Silva 2015)
R259	**Nagai K, Ochi F et al.**	Clinical characteristics and outcomes of chediak-Higashi syndrome: a nationwide survey of Japan	2013	Pediatric Blood & Cancer 60(10): 1582-1586 doi:10.1002/pbc.24637	0	0	no infectious agent mentioned
R260	**Nagy N, Matskova L et al.**	The apoptosis modulating role of SAP (SLAM associated protein) contributes to the symptomatology of the X linked lymphoproliferative disease	2009	Cell Cycle 8(19): 3086-3090 doi:10.4161/cc.8.19.9636	0	0	cell biology study
R261	**Naidoo R, Ungerer L et al.**	Primary immunodeficiencies: A 27-year review at a tertiary paediatric hospital in Cape Town, South Africa	2011	Journal of Clinical Immunology 31(1): 99-105 doi:10.1007/s10875-010-9465-7	0	0	no individual patient data
R262	**Naik S, Nicholas SK et al.**	Adoptive immunotherapy for primary immunodeficiency disorders with virus-specific T lymphocytes	2016	Journal of Allergy and Clinical Immunology 137(5): 1498-1505e1491 doi:10.1016/j.jaci.2015.12.1311	0	0	should maybe not have been excluded: a handful of fatal cases with infectious agents, but diagnosis may be not specific enough.
R263	**Narula S, LaRosa DF et al.**	Progressive multifocal leukoencephalopathy in a patient with common variable immunodeficiency and abnormal CD8+ T-cell subset distribution	2007	Annals of Allergy, Asthma and Immunology 98(5): 483-489 doi:10.1016/S1081-1206(10)60764-8	0	0	no genetic diagnosis and no clear gene candidate
R264	**Nazi N & Ladomenou F**	Gastrointestinal manifestations of primary immune deficiencies in children	2017	Int Rev Immunol 37(3): 111-118 doi:10.1080/08830185.2017.1365147	0	0	no individual patient data
R265	**Nevet MJ, Indelman M et al.**	A case of Netherton syndrome with intestinal atresia, a novel SPINK5 mutation, and a fatal course	2017	International Journal of Dermatology 56(10): 1055-1057 doi:10.1111/ijd.13730	0	0	no infectious agent mentioned
R266	**New HV, Cale CM et al.**	Nijmegen breakage syndrome diagnosed as fanconi anaemia	2005	Pediatric Blood and Cancer 44(5): 494-499 doi:10.1002/pbc.20271	0	0	no infectious agent mentioned
R267	**Niehues T, Reichenbach J et al.**	Nuclear factor κB essential modulator-deficient child with immunodeficiency yet without anhidrotic ectodermal dysplasia	2004	Journal of Allergy and Clinical Immunology 114(6): 1456-1462 doi:10.1016/j.jaci.2004.08.047	1	0	
R268	**Nielsen C, Jakobsen MA et al.**	Immunodeficiency associated with a nonsense mutation of IKBKB	2014	Journal of Clinical Immunology 34(8): 916-921	1	0	
R269	**Nielsen OH & LaCasse EC**	How genetic testing can lead to targeted management of XIAP deficiency-related inflammatory bowel disease	2017	Genetics in Medicine 19(2): 133-143 doi:10.1038/gim.2016.82	0	0	no infectious agent mentioned
R270	**Nikolajeva O, Worth A et al.**	Adenosine Deaminase Deficient Severe Combined Immunodeficiency Presenting as Atypical Haemolytic Uraemic Syndrome	2015	Journal of Clinical Immunology 35(4): 366-372 doi:10.1007/s10875-015-0158-0	1	0	
R271	**Nishimura G, Nakashima E et al.**	The Shwachman-Bodian-Diamond syndrome gene mutations cause a neonatal form of spondylometaphysial dysplasia (SMD) resembling SMD Sedaghatian type	2007	Journal of Medical Genetics 44(4): e73	0	0	SBDS mutations in two cases, girl did not die, boy died in utero.
R272	**Nistala K, Gilmour KC et al.**	X-linked lymphoproliferative disease: Three atypical cases	2001	Clinical and Experimental Immunology 126(1): 126-130 doi:10.1046/j.1365-2249.2001.01599.x	1	0	
R273	**Odio CD, Marciano BE et al.**	Risk Factors for Disseminated Coccidioidomycosis, United States	2017	Emerg Infect Dis 23(2): ? doi:10.3201/eid2302.160505	0	0	no fatality mentioned
R274	**Oh SH, Baek J et al.**	A synonymous variant in IL10RA affects RNA splicing in paediatric patients with refractory inflammatory bowel disease	2016	Journal of Crohn's and Colitis 10(11): 1366-1371 doi:10.1093/ecco-jcc/jjw102	0	0	no infectious agent mentioned
R275	**Okuno Y, Hoshino A et al.**	Late-Onset Combined Immunodeficiency with a Novel IL2RG Mutation and Probable Revertant Somatic Mosaicism	2015	Journal of Clinical Immunology 35(7): 610-614	1	0	
R276	**Oliveira PRS, Dessein H et al.**	IL2RA genetic variants reduce IL-2-dependent responses and aggravate human cutaneous leishmaniasis	2015	Journal of Immunology 194(6): 2664-2672 doi:10.4049/jimmunol.1402047	0	0	no fatality mentioned. Shows convincingly that certain mutations in the IL2R gene increases susceptibility to Leishmaniasis in a case control study with n > 100
R277	**Orange JS, Jain A et al.**	The presentation and natural history of immunodeficiency caused by nuclear factor κB essential modulator mutation	2004	Journal of Allergy and Clinical Immunology 113(4): 725-733 doi:10.1016/j.jaci.2004.01.762	2	0	
R278	**Orren A, Owen EP et al.**	Complete deficiency of the sixth complement component (C6Q0), susceptibility to Neisseria meningitidis infections and analysis of the frequencies of C6Q0 gene defects in South Africans	2012	Clinical and Experimental Immunology 167(3): 459-471 doi:10.1111/j.1365-2249.2011.04525.x	0	0	should not have been excluded: C6 deficiency. One patient died of N. meningitides and one of TB. 46 patients in total.

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R279	**Ørstavik KH, Kristiansen M et al.**	Novel splicing mutation in the NEMO (IKK-gamma) gene with severe immunodeficiency and heterogeneity of X-chromosome inactivation	2006	American Journal of Medical Genetics 140 A(1): 31-39 doi:10.1002/ajmg.a.31026	2	0	
R280	**Overwater E, Smulders Y et al.**	The value of DNA storage and pedigree analysis in rare diseases: a 17-year-old boy with X-linked lymphoproliferative disease (XLP) caused by a de novo SH2D1A mutation	2014	European Journal of Pediatrics 173(12): 1695-1698 doi:10.1007/s00431-014-2313-7	1	0	
R281	**Owen EP, Leisegang F et al.**	Complement component C5 and C6 mutation screening indicated in meningococcal disease in South Africa	2012	South African Medical Journal 102(6): 525-527	0	0	no individual data. Discusses if screening is useful for C5 or C6 deficiency in meningococcal disease in South Africa.
R282	**Ozsahin H, Arredondo-Vega FX et al.**	Adenosine deaminase deficiency in adults	1997	Blood 89(8): 2849-2855	1	0	
R283	**Ozsahin H, Le Deist F et al.**	Bone marrow transplantation in 26 patients with Wiskott-Aldrich syndrome from a single center	1996	Journal of Pediatrics 129(2): 238-244	0	0	should not have been excluded, 7 patients died post-BMT with infectious agent mentioned.
R284	**Pachlopnik Schmid J, Canioni D et al.**	Clinical similarities and differences of patients with X-linked lymphoproliferative syndrome type 1 (XLP-1/SAP deficiency) versus type 2 (XLP-2/XIAP deficiency)	2011	Blood 117(5): 1522-1529	0	0	should not have been excluded, 12 patients have an infectious agent and a fatal outcome, 5 have no mutational analysis but a clear gene suspect.
R285	**Padilla-Docal B, Dorta-Contreras AJ et al.**	Mannose-binding lectin deficiency with eosinophilic meningoencephalitis due to Angiostrongylus cantonensis in children: A case series	2011	Journal of Medical Case Reports 5(1): ? doi:10.1186/1752-1947-5-330	0	0	no fatality mentioned
R286	**Pannicke U, Baumann B et al.**	Deficiency of innate and acquired immunity caused by an IKBKB mutation	2013	New England Journal of Medicine 369(26): 2504-2514 doi:10.1056/NEJMoa1309199	2	0	
R287	**Park M, Yun YJ et al.**	Rotavirus-associated hemophagocytic lymphohistiocytosis (HLH) after hematopoietic stem cell transplantation for familial HLH	2015	Pediatrics International 57(2): e77-80	1	0	
R288	**Parolini O, Kagerbauer B et al.**	Analysis of SH2D1A mutations in patients with severe Epstein-Barr virus infections, Burkitt's lymphoma, and Hodgkin's lymphoma	2002	Annals of Hematology 81(8): 441-447 doi:10.1007/s00277-002-0490-3	0	0	no individual data available
R289	**Pasic S, Djuricic S et al.**	Recombinase-activating gene 1 immunodeficiency: different immunological phenotypes in three siblings	2009	Acta Paediatrica 98(6): 1062-1064	2	0	
R290	**Pasic S, Vujic D et al.**	Severe combined immunodeficiency in Serbia and Montenegro between years 1986 and 2010: A single-center experience	2014	Journal of Clinical Immunology 34(3): 304-308 doi:10.1007/s10875-014-9991-9	0	0	no individual data available
R291	**Patel SY, Doffinger R et al.**	Genetically determined susceptibility to mycobacterial infection	2008	Journal of Clinical Pathology 61(9): 1006-1012 doi:10.1136/jcp.2007.051201	0	0	no individual data available
R292	**Patiroglu T, Akar HH et al.**	Severe combined immunodeficiencies resulting from impaired purine metabolism: Single center experience	2016	Asim, Allerji, Immunoloji 14(1): 19-24 doi:10.21911/aai.5026	1	0	
R293 §	**Patiroglu T, Akar HH et al.**	X-linked severe combined immunodeficiency due to a novel mutation complicated with hemophagocytic lymphohistiocytosis and presented with invagination: a case report	2014	European Journal of Microbiology and Immunology 4(3): 174-6 doi:10.1556/EUJMI-D-14-00019	0	1	(1 single case cited by Akar 2016)
R294	**Patiroglu T, Akar HH et al.**	Partial Oculocutaneous Albinism and Immunodeficiency Syndromes: Ten Years Experience from a Single Center in Turkey	2016	Genetic Counseling 27(1): 67-76	0	0	no infectious agent mentioned
R295	**Pedraza-Sanchez S, Herrera-Barrios MT et al.**	Bacille Calmette-Guerin infection and disease with fatal outcome associated with a point mutation in the interleukin-12/interleukin-23 receptor beta-1 chain in two Mexican families	2010	International Journal of Infectious Diseases 14 Suppl 3(?): e256-260 doi:10.1016/j.ijid.2009.11.005	2	0	
R296	**Picard C & Casanova JL**	New primary immunodeficiency with infectious disease genetic predisposition	2003	Archives de Pediatrie 10(SUPPL. 4): 513s-516s doi:10.1016/S0929-693X(03)90059-5	0	0	no individual data
R297	**Picard C, Fieschi C et al.**	Inherited interleukin-12 deficiency: IL12B genotype and clinical phenotype of 13 patients from six kindreds	2002	American Journal of Human Genetics 70(2): 336-348 doi:10.1086/338625	1	0	
R298	**Picard C, Von Bernuth H et al.**	Clinical features and outcome of patients with IRAK-4 and MyD88 deficiency	2010	Medicine 89(6): 403-425 doi:10.1097/MD.0b013e3181fd8ec3	1	0	
R299	**Pienaar S, Eley BS et al.**	X-linked Hyper IgM (HIGM1) in an African kindred: The first report from South Africa	2003	BMC Pediatrics 3(1): ? doi:10.1186/1471-2431-3-12	1	0	
R300	**Poulin S, Corbeil C et al.**	Fatal Mycobacterium colombiense/cytomegalovirus coinfection associated with acquired immunodeficiency due to autoantibodies against interferon gamma: a case report	2013	BMC Infectious Diseases 13(?): 24	0	0	not PID: acquired immunodeficiency by antibodies against interferon gamma

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R301 §	**Pruszkowski A, Bourgault Villada I et al.**	Dermatophytic disease: role of type TC2 CD8 lymphocytes	1995	Ann Dermatol Venereol 122(Suppl 1): 55	0	1	(1 single case cited by Lanternier 2013)
R302	**Qamar F, Junejo S et al.**	A novel mutation in the JH4 domain of JAK3 causing severe combined immunodeficiency complicated by vertebral osteomyelitis	2017	Clinical Immunology 183(?): 198-200 doi:10.1016/j.clim.2017.09.007	0	0	no infectious agent mentioned
R303	**Quezada A, Norambuena X et al.**	Recurrent pneumonia as warning manifestation for suspecting primary immunodeficiencies in children	2001	Journal of Investigational Allergology and Clinical Immunology 11(4): 295-299	0	0	Many cases with infectious agents mentioned, but only 1 fatality with WAS which died of intracranial hemmorhage. No full-text available.
R304	**Rajyalakshmi R & Chakrapani RN**	Griscelli syndrome type 2: A rare and fatal syndrome in a South Indian boy	2016	Indian Journal of Pathology & Microbiology 59(1): 113-116	0	0	no fatality mentioned
R305	**Rambach G, Maier H et al.**	Complement induction and complement evasion in patients with cerebral aspergillosis	2008	Microbes and Infection 10(14-15): 1567-1576 doi:10.1016/j.micinf.2008.09.011	0	0	not PID, apparently Aspergillus can degrade C3 on its cell surface
R306	**Ramzan M, Yadav SP et al.**	Hemophagocytic lymphohistiocytosis in infants: a single center experience from India	2014	Pediatric Hematology & Oncology 31(3): 285-292 doi:10.3109/08880018.2013.862754	0	0	should not have been excluded: SCX11 gene with CMV infection, died of foscarnet-induced renal failure.
R307	**Rawat A, Singh S et al.**	Chronic granulomatous disease: two decades of experience from a tertiary care centre in North West India	2014	Journal of Clinical Immunology 34(1): 58-67	0	0	Infectious agents can only partially be matched to individual patients, need to contact author for more detail, but even now we can include 2 patients. Should not have been excluded
R308	**Read RC, Camp NJ et al.**	An interleukin-1 genotype is associated with fatal outcome of meningococcal disease	2000	Journal of Infectious Diseases 182(5): 1557-1560 doi:10.1086/315889	0	0	no individual patient data, but strong evidence for increased susceptibility with IL1B mutation for meningococcal disease. Should be included, but doesn't fit case extraction template.
R309	**Read RC, Cannings C et al.**	Variation within Genes Encoding Interleukin-1 and the Interleukin-1 Receptor Antagonist Influence the Severity of Meningococcal Disease	2003	Annals of Internal Medicine 138(7): 534-541+I539	0	0	Association study shows that the genotype at the interleukin-1 gene locus influences likelihood of survival of meningococcal disease but has no effect on susceptibility to the infection. Should be included, but doesn't fit case extraction template.
R310	**Regateiro FS, Belkaya S et al.**	Recurrent elevated liver transaminases and acute liver failure in two siblings with novel bi-allelic mutations of NBAS	2017	European Journal of Medical Genetics 60(8): 426-432 doi:10.1016/j.ejmg.2017.05.005	0	0	1 fatal case of NBAS deficiency, with infectious complications, but this case does not specify the pathogen (fatal pneumonia) and the second one mentions H1N1, parainfluenza 3, EBV, CMV, parvovirus B19 and H. pylori, but no fatality.
R311	**Régent A, Autran B et al.**	Idiopathic CD4 lymphocytopenia: Clinical and immunologic characteristics and follow-up of 40 patients	2014	Medicine (United States) 93(2): 61-72 doi:10.1097/MD.0000000000000017	0	0	No genetic diagnosis (idiopathic CD4 T-Lymphocytopenia), no clear gene candidate. 6 of 40 patients died, mostly of infections.
R312	**Reichenbach J, Schubert R et al.**	Impaired interferon-γ production in response to live bacteria and Toll-like receptor agonists in patients with ataxia telangiectasia	2006	Clinical and Experimental Immunology 146(3): 381-389 doi:10.1111/j.1365-2249.2006.03221.x	0	0	no fatalities mentioned, study on patient and control blood.
R313	**Rezaei N, Hedayat M et al.**	Primary immunodeficiency diseases associated with increased susceptibility to viral infections and malignancies	2011	Journal of Allergy and Clinical Immunology 127(6): 1329-1341.e1322 doi:10.1016/j.jaci.2011.02.047	0	0	narrative review
R314	**Rezai MS, Ahangarkani F et al.**	Evaluation of children with complication of BCG vaccination in North of Iran	2017	International Journal of Pediatrics 5(3): 4479-4488 doi:10.22038/ijp.2017.21886.1830	0	0	no individual patient data
R315	**Ricci S, Romano F et al.**	OL-EDA-ID Syndrome: a Novel Hypomorphic NEMO Mutation Associated with a Severe Clinical Presentation and Transient HLH	2017	Journal of Clinical Immunology 37(1): 7-11 doi:10.1007/s10875-016-0350-x	1	0	
R316	**Rice G, Patrick T et al.**	Clinical and molecular phenotype of Aicardi-Goutières syndrome	2007	American Journal of Human Genetics 81(4): 713-725 doi:10.1086/521373	0	0	PID that mimics congenital infection, in the absence of a pathogen.
R317	**Richter D, Hampl W & Pohlandt F**	Vertical transmission of cytomegalovirus, most probably by breast milk, to an infant with Wiskott-Aldrich syndrome with fatal outcome	1997	European Journal of Pediatrics 156(11): 854-855 doi:10.1007/s004310050729	0	0	should not have been excluded…
R318	**Rieber N, Gazendam RP et al.**	Extrapulmonary Aspergillus infection in patients with CARD9 deficiency	2016	JCI Insight 1(17): e89890 doi:10.1172/jci.insight.89890	1	0	
R319	**Rigaud C, Lebre AS et al.**	Natural history of Barth syndrome: a national cohort study of 22 patients	2013	Orphanet Journal Of Rare Diseases 8(?): 70	0	0	fatal infections do not specify which pathogen was involved.
R320	**Rigaud S, Fondanèche MC et al.**	XIAP deficiency in humans causes an X-linked lymphoproliferative syndrome	2006	Nature 444(7115): 110-114 doi:10.1038/nature05257	0	0	1 case of EBV-positive HLH with XIAP mutation should not have been excluded…

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R321	**Roberts CML, Angus JE et al.**	A novel NEMO gene mutation causing osteopetrosis, lymphoedema, hypohidrotic ectodermal dysplasia and immunodeficiency (OL-HED-ID)	2010	European Journal of Pediatrics 169(11): 1403-1407 doi:10.1007/s00431-010-1206-7	0	0	no fatalitity mentioned
R322	**Robertson N, Engelhardt KR et al.**	Astute Clinician Report: A Novel 10 bp Frameshift Deletion in Exon 2 of ICOS Causes a Combined Immunodeficiency Associated with an Enteritis and Hepatitis	2015	Journal of Clinical Immunology 35(7): 598-603 doi:10.1007/s10875-015-0193-x	1	0	
R323	**Rodrigues F, Graham Davies E et al.**	Liver disease in children with primary immunodeficiencies	2004	Journal of Pediatrics 145(3): 333-339 doi:10.1016/j.jpeds.2004.05.037	0	0	several fatal infection-related liver failures. Not clear if diagnosis is accurate enough in the sense of genetic diagnosis. Should maybe not have been excluded.
R324	**Rosen-Wolff A, Kreth HW et al.**	Periodic fever (TRAPS) caused by mutations in the TNFalpha receptor 1 (TNFRSF1A) gene of three German patients	2001	European Journal of Haematology 67(2): 105-109	0	0	1 fatality, but no infectious agent mentioned
R325	**Rozenbaum M & Rosner I**	Severe outcome of juvenile idiopathic arthritis (JIA) associated with familial Mediterranean fever (FMF)	2004	Clinical and Experimental Rheumatology 22(4 SUPPL. 34): S75-S78	0	0	no infectious complications mentioned
R326	**Rupert KL, Moulds JM et al.**	The molecular basis of complete complement C4A and C4B deficiencies in a systemic lupus erythematosus patient with homozygous C4A and C4B mutant genes	2002	Journal of Immunology 169(3): 1570-1578 doi:10.4049/jimmunol.169.3.1570	0	0	no infectious agent identified
R327	**Sadeghi-Shabestari M, Vesal S et al.**	Novel RAG2 mutation in a patient with T- B- severe combined immunodeficiency and disseminated BCG disease	2009	Journal of Investigational Allergology & Clinical Immunology 19(6): 494-496	2	0	
R328	**Salzer E, Daschkey S et al.**	Combined immunodeficiency with life-threatening EBV-associated lymphoproliferative disorder in patients lacking functional CD27	2013	Haematologica 98(3): 473-478 doi:10.3324/haematol.2012.068791	0	2	(2 cases cited from Alkhairy 2015, all others survived)
R329	**Sanal O, Ersoy F et al.**	Griscelli disease: Genotype-phenotype correlation in an array of clinical heterogeneity	2002	Journal of Clinical Immunology 22(4): 237-243 doi:10.1023/A:1016045026204	0	0	no infectious agents mentioned
R330	**Sanal O, Jing H et al.**	Additional diverse findings expand the clinical presentation of DOCK8 deficiency	2012	Journal of Clinical Immunology 32(4): 698-708 doi:10.1007/s10875-012-9664-5	0	0	two fatalities, but not infectious cause
R331	**Santadusit S, Visitsunthon N et al.**	X-linked hyper IgM syndrome: A report of the first case in Thailand with a confirmed mutation of CD40 ligand gene	2000	Asian Pacific Journal of Allergy and Immunology 18(3): 165-168	1	0	
R332	**Sanyal M, Morimoto M et al.**	Lack of IL7Rα expression in T cells is a hallmark of T-cell immunodeficiency in Schimke immuno-osseous dysplasia (SIOD)	2015	Clinical Immunology 161(2): 355-365 doi:10.1016/j.clim.2015.10.005	0	0	no fatalities mentioned, study on patient blood
R333	**Sarper N, Ipek IO et al.**	A rare syndrome in the differential diagnosis of hepatosplenomegaly and pancytopenia: report of identical twins with Griscelli disease	2003	Annals of Tropical Paediatrics 23(1): 69-73 doi:10.1179/000349803125002896	0	0	no infectious agent mentioned
R334	**Sato T, Kobayashi R et al.**	Stem cell transplantation in primary immunodeficiency disease patients	2007	Pediatrics International 49(6): 795-800 doi:10.1111/j.1442-200X.2007.02468.x	0	0	no fatalitymentioned
R335	**Savova R, Arshinkova M et al.**	Clinical case of immune dysregulation, polyendocrinopaty, enteropathy, X-linked (IPEX) syndrome with severe immune deficiency and late onset of endocrinopathy and enteropathy	2014	Case Reports in Medicine 2014(?): 564926 doi:10.1155/2014/564926	0	0	most infectious agents not mentioned, the one that was mentioned (candida) did not account for the fatality
R336	**Schepp J, Chou J et al.**	14 years after discovery: Clinical follow-up on 15 patients with inducible co-stimulator deficiency	2017	Frontiers in Immunology 8(AUG): 964 doi:10.3389/fimmu.2017.00964	0	0	one case of ICOS with HPV carcinoma should not have been excluded
R337	**Schober T, Magg T et al.**	A human immunodeficiency syndrome caused by mutations in CARMIL2	2017	Nature Communications 8(?): 14209 doi:10.1038/ncomms14209	0	0	several patients died of EBV-positive smooth muscle tumours, should not have been excluded
R338	**Schröder C, Baerlecken NT et al.**	Evaluation of RAG1 mutations in an adult with combined immunodeficiency and progressive multifocal leukoencephalopathy	2017	Clinical Immunology 179(?): 1-7 doi:10.1016/j.clim.2016.12.013	1	0	
R339	**Schuster V & Kreth HW**	X-linked lymphoproliferative disease is caused by deficiency of a novel SH2 domain-containing signal transduction adaptor protein	2000	Immunological Reviews 178(?): 21-28	0	0	narrative review
R340	**Schuster V, Hellebrand H et al.**	Mutation analysis of the sh2d1a/sap gene in 4 families affected by x-linked lymphoproliferative disease (xlp)	2000	Blood 96(11 PART I): 21a-21a	1	0	
R341	**Scott O, Kim VHD et al.**	Long-Term Outcome of Adenosine Deaminase-Deficient Patients—a Single-Center Experience	2017	Journal of Clinical Immunology 37(6): 582-591 doi:10.1007/s10875-017-0421-7	0	0	4 patients with ADA died post-treatment of infectious complications, should not have been excluded
R342	**Seidel MG, Boztug K & Haas OA**	Immune Dysregulation Syndromes (IPEX, CD27 Deficiency, and Others): Always Doomed from the Start?	2016	Journal of Clinical Immunology 36(1): 6-7	0	0	fatality only mentioned in family history with too little detail for inclusion

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R343	**Sell K, Storch K et al.**	Variable clinical course in acute necrotizing encephalopathy and identification of a novel RANBP2 mutation	2016	Brain and Development 38(8): 777-780 doi:10.1016/j.braindev.2016.02.007	0	0	no infectious agent mentioned
R344 §	**Serwas NK, Kansu A et al.**	Atypical manifestation of LRBA deficiency with predominant IBD-like phenotype.	2015	Inflamm Bowel Dis 21(1): 40-47 doi:10.1097/MIB.0000000000000266	0	1	(1 single case cited by Kostel 2017)
R345 §	**Seyama K, Nonoyama S et al.**	Mutations of the CD40 ligand gene and its effect on CD40 ligand expression in patients with X-linked hyper IgM syndrome	1998	Blood 92(7): 2421-34	0	2	(2 cases cited by Cabral-Marques 2014, although 1 could not be identified in the cited text. For the 10 fatalities listed, no infectious causes are mentioned.)
R346	**Sfaihi L, Aloulou H et al.**	Primary immunodeficiency disorders in 51 cases	2013	Tunisie Medicale 91(1): 38-43	0	0	no individual patient data
R347	**Sfaihi L, Stoppa Lyonnet D et al.**	Ataxia-telangiectasia in the south of Tunisia: A study of 11 cases	2015	La Tunisie médicale 93(8-9): 511-515	0	0	no individual patient data
R348	**Shabestari MS, Maljaei SH et al.**	Distribution of primary immunodeficiency diseases in the Turk ethnic group, living in the northwestern Iran	2007	Journal of Clinical Immunology 27(5): 510-516 doi:10.1007/s10875-007-9101-3	0	0	no individual data on infectious events (15 infectious fatalities, not clear which patients)
R349	**Shanon A, Levin S et al.**	Combined familial adenosine deaminase and purine nucleoside phosphorylase deficiencies	1988	Archives of Disease in Childhood 63(8): 931-934	0	0	no infectious agent identified
R350	**Sharapova SO, Chang EY et al.**	Next generation sequencing revealed DNA ligase IV deficiency in a "developmentally normal" patient with massive brain Epstein-Barr virus-positive diffuse large B-cell lymphoma	2016	Clinical Immunology 163(?): 108-110 doi:10.1016/j.clim.2016.01.002	0	0	EBV-positive fatal lymphoma with LIG4 mutation. Should not have been excluded
R351	**Sharfe N, Nahum A et al.**	Fatal combined immunodeficiency associated with heterozygous mutation in STAT1	2014	Journal of Allergy and Clinical Immunology 133(3): 807-817 doi:10.1016/j.jaci.2013.09.032	3	0	
R352	**Shimoda K, Mimaki M et al.**	Brain edema with clasmatodendrosis complicating ataxia telangiectasia	2017	Brain and Development 39(7): 629-632 doi:10.1016/j.braindev.2017.02.007	0	0	no infectious agent mentioned
R353	**Singh A, Bryan MM et al.**	A clinical report of Chediak-Higashi syndrome in infancy with a novel genotype from the Indian subcontinent	2016	International Journal of Dermatology 55(3): 317-321 doi:10.1111/ijd.13019	0	0	no fatality mentioned
R354	**Sjoholm AG, Braconier JH & Soderstrom C**	Properdin deficiency in a family with fulminant meningococcal infections	1982	Clinical and Experimental Immunology 50(2): 291-297	3	0	
R355	**Sologuren I, Boisson-Dupuis S et al.**	Partial recessive IFN-γR1 deficiency: Genetic, immunological and clinical features of 14 patients from 11 kindreds	2011	Human Molecular Genetics 20(8): 1509-1523 doi:10.1093/hmg/ddr029	1	0	
R356	**Spinner MA, Ker JP et al.**	GATA2 deficiency underlying severe blastomycosis and fatal herpes simplex virus-associated hemophagocytic lymphohistiocytosis	2016	Journal of Allergy & Clinical Immunology 137(2): 638-640 doi:10.1016/j.jaci.2015.07.043	1	0	
R357	**Spinner MA, Sanchez LA et al.**	GATA2 deficiency: a protean disorder of hematopoiesis, lymphatics, and immunity	2014	Blood 123(6): 809-821	6	0	(1 additional case with qeustionable link between fatality and mentioned pathogens in list of cases with issues)
R358	**Sprong T, Roos D et al.**	Deficient alternative complement pathway activation due to factor D deficiency by 2 novel mutations in the complement factor D gene in a family with meningococcal infections	2006	Blood 107(12): 4865-4870 doi:10.1182/blood-2005-07-2820	0	0	Fatal N.meinigitis case of survived sibling with CFD mutation in consangious family. Should not have been excluded.
R359	**Standen GR, Orchard JA & Hutton RD**	Wiskott-Aldrich syndrome: Fatal consequences of splenectomy in an unrecognised attenuated variant	1990	British Journal of Clinical Practice 44(8): 338-339	1	0	
R360	**Stapleton FB, Linshaw MA & Cuppage FE**	The alternate complement pathway. A possible role in a patient with focal glomerular sclerosis	1981	Archives of Pathology and Laboratory Medicine 105(3): 160-163	0	0	no fatality mentioned
R361	**Steele RW, Britton HA et al.**	Severe combined immunodeficiency with cartilage- hair hypoplasia: In vitro response to thymosin and attempted reconstitution	1976	Pediatric Research 10(12): 1003-1005 doi:10.1203/00006450-197612000-00012	0	0	no genetic diagnosis (SCID) and no clear gene candidate
R362	**Sterlin D, Velasco G et al.**	Genetic, Cellular and Clinical Features of ICF Syndrome: a French National Survey	2016	Journal of Clinical Immunology 36(2): 149-159 doi:10.1007/s10875-016-0240-2	0	0	no infectious agent mentioned
R363	**Stojanov S, Dejaco C et al.**	Clinical and functional characterisation of a novel TNFRSF1A c.605T>A/V173D cleavage site mutation associated with tumour necrosis factor receptor-associated periodic fever syndrome (TRAPS), cardiovascular complications and excellent response to etanercep	2008	Annals of the Rheumatic Diseases 67(9): 1292-1298 doi:10.1136/ard.2007.079376	0	0	no infectious agent mentioned
R364	**Strickler A, Gallo S et al.**	Leucocyte adhesion deficiency type 1 with developmental delay secondary to CMV infection and filiation questions	2015	BMJ Case Reports 2015(apr09 1): bcr2014208973-bcr2014208973 doi:10.1136/bcr-2014-208973	1	0	

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R365	**Suliaman F, Al-Ghonaium A & Harfi H**	High incidence of severe combined immune deficiency in the Eastern Province of Saudi Arabia	2006	Pediatric Asthma, Allergy and Immunology 19(1): 14-18 doi:10.1089/pai.2006.19.14	0	0	no individual patient data
R366	**Sun J, Ying W et al.**	Clinical and Genetic Features of 5 Chinese Patients with X-linked lymphoproliferative Syndrome	2013	Scandinavian Journal of Immunology 78(5): 463-467 doi:10.1111/sji.12103	3	0	
R367	**Sun-Tan C, Turul Özgür T et al.**	Hereditary C1q deficiency: A new family with C1qA deficiency	2010	Turkish Journal of Pediatrics 52(2): 184-186	0	0	no fatality mentioned
R368	**Suri D, Singh S et al.**	Clinical profile and genetic basis of Wiskott-Aldrich syndrome at Chandigarh, North India	2012	Asian Pacific Journal of Allergy and Immunology 30(1): 71-78	2	0	
R369	**Szczawinska-Poplonyk A, Kycler Z et al.**	Pulmonary lymphomatoid granulomatosis in Griscelli syndrome type 2	2011	Viral Immunology 24(6): 471-473 doi:10.1089/vim.2011.0034	1	0	
R370	**Takada H, Ishimura M et al.**	Invasive Bacterial Infection in Patients with Interleukin-1 Receptor-associated Kinase 4 Deficiency: Case Report	2016	Medicine 95(4): e2437	5	0	
R371	**Takano T, Zielenska M & Becker LE**	Cytomegalovirus encephalitis in a child with adenosine deaminase-deficient severe combined immune deficiency: a neuropathologic study	1998	Neuropediatrics 29(3): 151-154	1	0	
R372	**Tezcan I, Ersoy F et al.**	A case of adenosine deaminase-negative severe combined immunodeficiency with neurological abnormalities	1995	Turkish Journal of Pediatrics 37(4): 383-389	0	0	Infection (pneumonia with respiratory failure), but no specific infectious agent mentioned
R373	**Tong YH, Sinniah D et al.**	Two Malaysian Chinese male children with the Wiskott-Aldrich syndrome	1979	Singapore Medical Journal 20(2): 355-359	0	0	Fatal pseudomonas septicemia with WAS (no genetic diagnosis). Should probably not have been excluded.
R374	**Toyoda H, Ido M et al.**	Multiple cutaneous squamous cell carcinomas in a patient with interferon γ receptor 2 (IFNγR2) deficiency	2010	Journal of Medical Genetics 47(9): 631-634 doi:10.1136/jmg.2009.072108	1	0	
R375	**Trakultivakorn M & Ochs HD**	X-linked agammaglobulinemia in Northern Thailand	2006	Asian Pacific Journal of Allergy and Immunology 24(1): 57-63	1	0	
R376	**Treon SP, Cao Y et al.**	Somatic mutations in MYD88 and CXCR4 are determinants of clinical presentation and overall survival in Waldenström macroglobulinemia	2014	Blood 123(18): 2791-2796 doi:10.1182/blood-2014-01-550905	0	0	no individual patient data
R377	**Triki C, Feki I et al.**	Clinical, biological and genetic study of 24 patients with ataxia telangiectasia from southern Tunisia	2000	Revue Neurologique 156(6-7): 634-637	0	0	no individual patient data
R378	**Tsai HY, Yu HH et al.**	X-linked hyper-IgM syndrome with CD40LG mutation: two case reports and literature review in Taiwanese patients	2015	Journal of Microbiology, Immunology & Infection 48(1): 113-118 doi:10.1016/j.jmii.2012.07.004	1	0	
R379 §	**Tsuge I, Matsuoka H et al.**	Necrotizing toxoplasmic encephalitis in a child with the X-linked hyper-IgM syndrome	1998	Eur J Pediatr 157(): 735-737	0	1	(1 single case cited by Liu 2017)
R380	**Tsuji Y, Imai K et al.**	Hematopoietic stem cell transplantation for 30 patients with primary immunodeficiency diseases: 20 years experience of a single team	2006	Bone Marrow Transplantation 37(5): 469-477	7	0	(1 case without genetic diagnosis in list of cases with issues)
R381	**Tsukerman P, Eisenstein EM et al.**	Cytokine secretion and NK cell activity in human ADAM17 deficiency	2015	Oncotarget 6(42): 44151-44160	0	0	no infectious agent mentioned
R382	**Turul T, Tezcan I et al.**	Clinical heterogeneity can hamper the diagnosis of patients with ZAP70 deficiency	2009	European Journal of Pediatrics 168(1): 87-93 doi:10.1007/s00431-008-0718-x	0	0	no infectious agent mentioned
R383	**Uckan D, Cetin M et al.**	Pneumatosis intestinalis in an infant undergoing bone marrow transplantation for Wiskott-Aldrich syndrome	2001	Pediatric Transplantation 5(5): 370-373	0	0	Fatal K.pneumonia sepsis with WAS. Should probably not have been excluded.
R384	**Vairo D, Tassone L et al.**	Severe impairment of IFN-γ and IFN-α responses in cells of a patient with a novel STAT1 splicing mutation	2011	Blood 118(7): 1806-1817 doi:10.1182/blood-2011-01-330571	0	0	no fatality mentioned
R385	**Van Der Crabben SN, Hennus MP et al.**	Destabilized SMC5/6 complex leads to chromosome breakage syndrome with severe lung disease	2016	Journal of Clinical Investigation 126(8): 2881-2892 doi:10.1172/JCI82890	0	0	no infectious agent mentioned
R386	**van Montfrans JM, Hoepelman AI et al.**	CD27 deficiency is associated with combined immunodeficiency and persistent symptomatic EBV viremia	2012	Journal of Allergy & Clinical Immunology 129(3): 787-793.e786 doi:10.1016/j.jaci.2011.11.013	0	1	(1 case cited by Alkhairy 2015)
R387	**van Montfrans JM, Rudd E et al.**	Fatal hemophagocytic lymphohistiocytosis in X-linked chronic granulomatous disease associated with a perforin gene variant	2009	Pediatric Blood & Cancer 52(4): 527-529 doi:10.1002/pbc.21851	1	0	
R388	**Vatanavicharn N, Visitsunthorn N et al.**	An infant with cartilage-hair hypoplasia due to a novel homozygous mutation in the promoter region of the RMRP gene associated with chondrodysplasia and severe immunodeficiency	2010	Journal of Applied Genetics 51(4): 523-528	0	0	no fatality mentioned

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R389 §	**Vinurel H, Freymond N et al.**	Le syndrome de Whim : une cause exceptionnelle de bronchiectasies diffuses	2008	Rev Mal Respir 25(5): 614-18 doi:10.1019/200720265	0	1	(1 single case cited by Beaussant 2012)
R390	**Voskoboinik I & Trapani JA**	Perforinopathy: A spectrum of human immune disease caused by defective perforin delivery or function	2013	Frontiers in Immunology 4(DEC): 441 doi:10.3389/fimmu.2013.00441	0	0	narrative review
R391	**Wada T, Sakakibara Y et al.**	Down-regulation of CD5 expression on activated CD8+ T cells in familial hemophagocytic lymphohistiocytosis with perforin gene mutations	2013	Human Immunology 74(12): 1579-1585 doi:10.1016/j.humimm.2013.09.001	0	0	no infectious agent mentioned
R392 §	**Wan C, Yu HH et al.**	Clinical manifestations and outcomes of pediatric chronic neutropenia	2012	J Formos Med Assoc 111(): 220-227	0	1	(1 single case cited by Lee 2013)
R393	**Wessell KR, Tcheurekdjian H & Hostoffer R**	Autosomal dominant transmission of signal transduction and activator of transcription 1 (STAT1) mutation (Thr385Met) and extended lifespan	2016	LymphoSign Journal 3(1): 13-17 doi:10.14785/lpsn-2015-0013	1	0	
R394	**Winkelstein JA, Marino MC et al.**	The X-Linked Hyper-IgM Syndrome: Clinical and Immunologic Features of 79 Patients	2003	Medicine 82(6): 373-384 doi:10.1097/01.md.0000100046.06009.b0	0	0	no individual patient data
R395	**Winkelstein JA, Marino MC et al.**	X-linked agammaglobulinemia: report on a United States registry of 201 patients	2006	Medicine 85(4): 193-202 doi:10.1097/01.md.0000229482.27398.ad	0	0	no individual patient data
R396	**Wolska-Kusnierz B, Bajer A et al.**	Cryptosporidium infection in patients with primary immunodeficiencies	2007	Journal of Pediatric Gastroenterology & Nutrition 45(4): 458-464 doi:10.1097/MPG.0b013e318054b09b	1	0	(1 additional case without genetic diagnosis in list of cases with issues)
R397	**Woutsas S, Aytekin C et al.**	Hypomorphic mutation in TTC7A causes combined immunodeficiency with mild structural intestinal defects	2015	Blood 125(10): 1674-1676 doi:10.1182/blood-2014-08-595397	0	0	no infectious agent mentioned
R398	**Wu J, Chen J et al.**	Clinical Manifestations and Genetic Analysis of 17 Patients with Autosomal Dominant Hyper-IgE Syndrome in Mainland China: New Reports and a Literature Review	2017	Journal of Clinical Immunology 37(2): 166-179 doi:10.1007/s10875-017-0369-7	1	0	
R399	**Wu J, Wang WF et al.**	Clinical Features and Genetic Analysis of 48 Patients with Chronic Granulomatous Disease in a Single Center Study from Shanghai, China (2005-2015): New Studies and a Literature Review	2017	Journal of Immunology Research 2017(?): ? doi:10.1155/2017/8745254	2	0	(2 additional cases with unclear link of mentioned pathogen and fatal complication in list of cases with issues).
R400	**Xavier-da-Silva MM, Moreira-Filho CA et al.**	Fetal-onset IPEX: Report of two families and review of literature	2015	Clinical Immunology 156(2): 131-140 doi:10.1016/j.clim.2014.12.007	3	0	
R401	**Xu H, Tian W et al.**	Clinical and Molecular Features of 38 Children with Chronic Granulomatous Disease in Mainland China	2014	Journal of Clinical Immunology 34(6): 633-641 doi:10.1007/s10875-014-0061-0	0	0	no individual patient data, not clear which 17 patients died. Not all patients had CYBB mutations.
R402	**Xu S, Li Q et al.**	Identification of IL2RG and CYBB mutations in two Chinese primary immunodeficiency patients by whole-exome sequencing	2018	Immunol Invest 47(3): 221-228 doi:10.1080/08820139.2017.1371186	0	0	no infectious agent mentioned
R403	**Yang X, Kanegane H et al.**	Clinical and genetic characteristics of XIAP deficiency in Japan	2012	Journal of Clinical Immunology 32(3): 411-420 doi:10.1007/s10875-011-9638-z	0	0	no infectious agent mentioned
R404	**Yang YL, Lu MY et al.**	Hematopoietic stem cell transplantation in Taiwanese children with primary immunodeficiency	2005	Journal of the Formosan Medical Association 104(2): 101-106	0	0	(2 cases without genetic diagnosis in list of cases with issues).
R405	**Yao CM, Han XH et al.**	Clinical characteristics and genetic profiles of 44 patients with severe combined immunodeficiency (SCID): Report from Shanghai, China (2004-2011)	2013	Journal of Clinical Immunology 33(3): 526-539 doi:10.1007/s10875-012-9854-1	0	0	no infectious agents mentioned
R406	**Yee A, De Ravin SS et al.**	Severe combined immunodeficiency: A national surveillance study	2008	Pediatric Allergy and Immunology 19(4): 298-302 doi:10.1111/j.1399-3038.2007.00646.x	0	0	no individual patient data
R407	**Yen TY, Hwu WL et al.**	Acute metabolic decompensation and sudden death in Barth syndrome: report of a family and a literature review	2008	European Journal of Pediatrics 167(8): 941-944	0	0	no fatality mentioned
R408	**Yetgin S, Olcay L et al.**	Transformation of severe congenital neutropenia to early acute lymphoblastic leukemia in a patient with HAX1 mutation and without G-CSF administration or receptor mutation	2008	Leukemia 22(9): 1797	0	0	no infectious agent mentioned
R409	**Yoshioka T, Nishikomori R et al.**	Autosomal dominant anhidrotic ectodermal dysplasia with immunodeficiency caused by a novel NFKBIA mutation, p.Ser36Tyr, presents with mild ectodermal dysplasia and non-infectious systemic inflammation	2013	Journal of Clinical Immunology 33(7): 1165-1174	0	0	no infectious agent mentioned
R410	**Zeng H, Tao Y et al.**	Primary immunodeficiency in South China: Clinical features and a genetic subanalysis of 138 children	2013	Journal of Investigational Allergology and Clinical Immunology 23(5): 302-308	0	0	no individual patient data on outcome

#	Authors	Title	Year	Reference	Cases	Cited	Reason for exclusion
R411	**Zheng F, Li J et al.**	ITK Gene Mutation: Effect on Survival of Children with Severe Hemophagocytic Lymphohistiocytosis	2016	Indian J Pediatr 83(11): 1349-1352 doi:10.1007/s12098-016-2079-1	3	0	
R412	**Ziegler JB, Lee CH & Van Der Weyden MB**	Severe combined immunodeficiency and adenosine deaminase deficiency: Failure of enzyme replacement therapy	1980	Archives of Disease in Childhood 55(6): 452-457	1	0	

11.7. Appendix G – Table 9: Extracted cases (without patient history)

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P1	Bhattacharya A, Slatter MA et al. (2005)		5	f	ADA	not indicated	HPIV-3	likely
P2	Nikolajeva O, Worth A et al. (2015)		4	m	ADA	Homozygous (splice site mutation) c.975 -1G > C	Fungi	likely
P3	Ozsahin H, Arredondo-Vega FX et al. (1997)		1	f	ADA	missense mutation G216R and P126Q	JCPyV	likely
P4	Patiroglu T, Akar HH et al. (2016)		Case 1	m	ADA	homozygous nonsense mutation (c.736C>T, p.Q246X) in exon 8	HCMV, Candida	likely
P5	Takano T, Zielenska M & Becker LE (1998)		male infant	m	ADA?	Cultured skin fibroblasts were used to confirm a diagnosis of ADA.	HCMV	likely
P6	Ziegler JB, Lee CH & Van Der Weyden MB (1980)		Pat	m	ADA?	clinical diagnosis of ADA deficiency	Parainfluenza	likely
P7	Bandsma RH, van Goor H et al. (2015)	Blaydon DC, Biancheri P et al. (2011)	girl	f	ADAM17	homozygous new deletion of 4 bp in exon 5 of ADAM17 (c.603– 606delCAGA) on chromosome 2, p.Asp201GlufsX11	PVB19	likely
P8	Bandsma RH, van Goor H et al. (2015)		index	f	ADAM17	homozygous NM_003183.4:c.308dupA, p.Asn103LysfsTer20	HRSV	likely
P9	Enders A, Zieger B et al. (2006)		index	m	AP3B1	homozygous NM_003664 c.1029A>T p.R302X. Additionally a heterozygous RAB27A NM_183234 paternally inherited mutation (Del381, 382AG, Ins381C) leading to a stop codon at AS 84.	EBV, HCMV	possible
P10	Mortaz E, Marashian SM et al. (2017)		Girl	f	ATM	novel mutation (c.3244_3245insG; p.His1082fs)	EBV	possible
P11	Asgari S, McLaren PJ et al. (2016)		S4	m	BTK	Frameshift in position 100617192 (X chromosome) C > CT	P. aeruginosa, HHV6	likely
P12	Kanegane H, Taneichi H et al. (2005)		P13	?	BTK	861insCT, I243ins277X	P. aeruginosa	likely
P13	Kanegane H, Taneichi H et al. (2005)		P4	?	BTK	1925delAT, Y598X	P. aeruginosa	likely
P14	Lee KH, Shyur SD et al. (2011)		4	m	BTK	c.1106 T>C (p.L369P)	P. aeruginosa	likely
P15	Lee WI, Kuo ML et al. (2005)		4	m	BTK	1694A > T (exon 15) Asp 521 Val	S. pneumoniae, S. aureus, HBV	likely
P16	Trakultivakorn M & Ochs HD (2006)		Pat 2	m	BTK	missense mutation (exon 19) 2075T>C (Leuk648Pro)	S. pneumoniae	likely
P17	Marquart HV, Schejbel L et al. (2007)		Patient	f	C1QB	novel missense mutation (Gly-Arg) in codon 217 of the B chain	P. carinii	likely
P18	Jönsson G, Truedsson L et al. (2005)		4	f	C2	thirty-three persons with C2D were found to be homozygous for the 28-bp deletion34 and were also homozy- gous for DRB1*15 and C4A*4 B*2	S. aureus	likely
P19	Jönsson G, Truedsson L et al. (2005)		12	m	C2	thirty-three persons with C2D were found to be homozygous for the 28-bp deletion34 and were also homozy- gous for DRB1*15 and C4A*4 B*2	S. pneumoniae	likely
P20	Jönsson G, Truedsson L et al. (2005)		39	f	C2	thirty-three persons with C2D were found to be homozygous for the 28-bp deletion34 and were also homozy- gous for DRB1*15 and C4A*4 B*2	S. pneumoniae	likely
P21	Glockel U, Schneider PM et al. (1990)		Patientin	f	C2?	Immunochechemically marked plasma of the patient in western blot showed complete absence of C2 protein, in contrast to heterozygote parents and normal controls	S. pneumoniae	likely
P22	Grace HJ, Brereton Stiles GG et al. (1976)		White girl	f	C3?	clinical diagnosis	S. pneumoniae	likely

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P23	Lanternier F, Pathan S et al. (2013)		9	m	CARD9	mutation analysis not done (likely Q289X/Q289X)	Fungi	likely
P24	Lanternier F, Pathan S et al. (2013)	Boudghène-Stambouli O & Mérad-Boudia A (1998)	10	m	CARD9	c.865 C>T, p.Q289X/Q289X	T. violaceum	likely
P25	Lanternier F, Pathan S et al. (2013)	Boudghène-Stambouli O & Mérad-Boudia A (1990)	2	m	CARD9	not available (likely Q289X/Q289X)	T. violaceum	likely
P26	Lanternier F, Pathan S et al. (2013)	Pruszkowski A, Bourgault Villada I et al. (1995)	5 (Monsieur M. in Pruszkoswki)	m	CARD9	mutation analysis not done (likely Q289X/Q289X, same as 1 brother and 1 sister)	T. violaceum	possible
P27	Rieber N, Gazendam RP et al. (2016)		Patient 2	m	CARD9	homozygous mutation in the start codon, c.3G>C, p.M1I	A. fumigatus	possible
P28	Fuchs S, Rensing-Ehl A et al. (2015)		P1	f	CARD11	homozygous germline mutation c.450T>A leading to a premature stop codon. Additionally in some cell populations c.499G>T, leading to p.Cys150Leu instead of p.Cys150*	S. aureus, Enterococcus, P. aeruginosa, HCMV, Metapneumovirus, Rhinovirus	likely
P29	Fuchs S, Rensing-Ehl A et al. (2015)		P2	m	CARD11	homozygous germline mutation c.450T>A p.Cys150*	Enterococcus, Klebsiella, HCMV	likely
P30	Alkhairy OK, Perez-Becker R et al. (2015)	Salzer E, Daschkey S et al. (2013)	P10 from Melbourne; P8 in Salzer	f	CD27	homozygous c.G158A, p.C53Y	EBV	possible
P31	Alkhairy OK, Perez-Becker R et al. (2015)		P15	f	CD27	homozygous c.G287A, p.C96Y	Candida, CoxV, T. gondii	possible
P32	Alkhairy OK, Perez-Becker R et al. (2015)		P17	f	CD27	homozygous c.C232T, p.R78W	EBV	likely
P33	Alkhairy OK, Perez-Becker R et al. (2015)	van Montfrans JM, Hoepelman AI et al. (2012)	P2 (from Utrecht); An older brother in van Montfrans	m	CD27	homozygous c.G24A, p.W8X	EBV, GPB	likely
P34	Alkhairy OK, Perez-Becker R et al. (2015)	Salzer E, Daschkey S et al. (2013)	P9 from Melbourne; P7 in Salzer	f	CD27	homozygous c.G158A, p.C53Y	EBV	possible
P35	Al-Saud BK, Al-Sum Z et al. (2013)		7	m	CD40	N/A	P. aeruginosa	likely
P36	Al-Saud BK, Al-Sum Z et al. (2013)		4c	f	CD40	c.256+2 T>C (splice site) homozygous	Cryptosporidium	likely
P37	Cabral-Marques O, Klaver S et al. (2014)	Seyama K, Nonoyama S et al. (1998)	16; Seyama: TA?	?	CD40LG	c.817C>T p.T254M	HCMV, G. lamblia, I. belli	likely
P38	Cabral-Marques O, Klaver S et al. (2014)	Seyama K, Nonoyama S et al. (1998)	9; Seyama: MS?	?	CD40LG	splice site c.345_402del 58bp skipping exon 3	K. pneumoniae, Acinetobacter	possible
P39	Lee WI, Chen CC et al. (2017)		HIGM3-CD40L	m	CD40LG	c.526 T>A, p.Tyr169Asn	E. coli, CoxV	likely
P40	Lee WI, Huang JL et al. (2013)	Wan C, Yu HH et al. (2012)	F; could not be identified in Wan	m	CD40LG	nonsense, G 476 ->A exon 5 Try 140 stop, TNF-H	S. pneumoniae, P. aeruginosa, Candida	likely
P41	Liu X, Zhou K et al. (2017)		this report	m	CD40LG	c.654C>A (p.C218X)	T. gondii	likely
P42	Liu X, Zhou K et al. (2017)	Tsuge I, Matsuoka H et al. (1998)	Tsuge : single case	?	CD40LG	V237E	T. gondii	likely
P43	Lu G & Yu D (2017)		Case report	m	CD40LG	homozygous C to A substitution in exon 5 (c.654C>A)	T. gondii	likely
P44	Pienaar S, Eley BS et al. (2003)		Patient 2	?	CD40LG	Deletion in exon 3	Cryptococcus	possible
P45	Santadusit S, Visitsunthon N et al. (2000)		A.S.	m	CD40LG	point mutation of exon 5 (A619T)	P. aeruginosa	likely

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P46	Tsai HY, Yu HH et al. (2015)		Case 1	m	CD40LG	Exon 5 at nucleotide position 476 (cDNA 476G > A)	P. aeruginosa, Candida	likely
P47	Tsuji Y, Imai K et al. (2006)		Pat 23	m	CD40LG	Confirmed by mutational analysis	C. parvum, P. aeruginosa	likely
P48	Tsuji Y, Imai K et al. (2006)		Pat 25	m	CD40LG	Confirmed by mutational analysis	Aspergillus	likely
P49	Wolska-Kusnierz B, Bajer A et al. (2007)		Patient 2	m	CD40LG	point mutation at 253bp of exon 5	C. parvum	likely
P50	Mancebo E, Moreno-Pelayo MA et al. (2008)	de la Calle-Martin O, Hernandez M et al. (2001)	II.1 in family 1; index patient in de la Calle	m	CD8A	homozygous c.331G>A (exon 2), p.Gly111Ser (accession number AY039664)	P. aeruginosa	possible
P51	Sjoholm AG, Braconier JH & Soderstrom C (1982)		Case 1 (III:10)	m	CFP?	Properdin was undetectable in serum and plasma by electroimmunoassay.	N. meningitidis C	likely
P52	Sjoholm AG, Braconier JH & Soderstrom C (1982)		Case 2 (III:8)	m	CFP?	Properdin was undetectable in his brother's serum (III:10) serum and plasma by electroimmunoassay.	N. meningitidis	likely
P53	Sjoholm AG, Braconier JH & Soderstrom C (1982)		Case 3 (II:5)	m	CFP?	Properdin was undetectable in serum and plasma by electroimmunoassay.	N. meningitidis	likely
P54	Beaussant Cohen S, Fenneteau O et al. (2012)		5231	f	CXCR4	c.1013C>G p.S338X	HCMV, P. aeruginosa, HPV	likely
P55	Beaussant Cohen S, Fenneteau O et al. (2012)	Vinurel H, Freymond N et al. (2008)	5446	m	CXCR4	c.1013C>G p.S338X	Mycobacterium	likely
P56	Lee WI, Chen CC et al. (2017)		CGD3-gp91	m	CYBB	c.1249 C>A, p.Thr343Lys (Gen wird als gp91 bezeichnet)	Salmonella, Aspergillus, BCG	likely
P57	van Montfrans JM, Rudd E et al. (2009)		3.5-year-old male	m	CYBB	homozygous c.676C>T p.Arg226stop. Additionally heteroygous p.Asp491Asn substitution in the perforin (PRF1) gene.	B. cepacia, S. maltophilia	likely
P58	Wu J, Wang WF et al. (2017)		P13	m	CYBB	Deletion Exon 10, c.1314delG, p.I439SfsX62	A. baumannii	likely
P59	Wu J, Wang WF et al. (2017)		P3	m	CYBB	Missense Exon 5, c.466G>A, p.A156T	TB	likely
P60	Lee PP, Woodbine L et al. (2013)		P1.1	f	DCLRE1C	Compound heterozygous exon 1–3 deletion, p.Thr71Pro	Aspergillus	possible
P61	Lee PP, Woodbine L et al. (2013)	Moshous D, Pannetier C et al. (2003)	P3.1; P68 in Moshous	m	DCLRE1C	Compound heterozygous exon 1–3 deletion, p.Asp451LysfsX11	EBV	possible
P62	Lee PP, Woodbine L et al. (2013)	Moshous D, Pannetier C et al. (2003)	P3.2; P69 in Moshous	f	DCLRE1C	Compound heterozygous exon 1–3 deletion, p.Asp451LysfsX11	EBV	possible
P63	Lee PP, Woodbine L et al. (2013)	Moshous D, Pannetier C et al. (2003)	P3.3; P70 in Moshous	f	DCLRE1C	Compound heterozygous exon 1–3 deletion, p.Asp451LysfsX11	T. gondii	likely
P64	Lee PP, Woodbine L et al. (2013)	Moshous D, Pannetier C et al. (2003)	P4; P72 in Moshous	f	DCLRE1C	Homozygous p.Thr432SerfsX16	Cryptosporidium	possible
P65	Lee PP, Woodbine L et al. (2013)	Ege M, Ma Y et al. (2005)	P5.2; second boy in Ege	m	DCLRE1C?	not tested, but youngest brother has compound heterozygous p.Met1Thr, p.His35Asp	Aspergillus	likely
P66	Lin JH, Yu-Yun Lee J et al. (2002)		The patient	m	DKC1	c.1058C>T (p.A353V) (sample from mother)	E. coli	likely
P67	Asgari S, McLaren PJ et al. (2016)		S13	m	DNMT3B	In-frame deletion of 6 base pairs in position 31393171 (chromosome 20) ACTCGAG > A	P. aeruginosa, VZV	likely
P68	Hagleitner MM, Lankester A et al. (2008)		15	m	DNMT3B	V726G/V726G	Klebsiella	likely

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P69	Hagleitner MM, Lankester A et al. (2008)		29	f	DNMT3B	STP807ins/STP807ins	Klebsiella, P. jirovecii	likely
P70	Dobbs K, Dominguez Conde C et al. (2015)		P3	m	DOCK2	homozygous g.169145781G>T p.Arg751Ser	VZV	likely
P71	Dobbs K, Dominguez Conde C et al. (2015)		P4	m	DOCK2	homozygous g.169145756_169145757dup(TG) p.Phe744fs	K. pneumoniae, BCG, HPIV-3, HAdV, HCMV	likely
P72	Alsum Z, Hawwari A et al. (2013)		F2P1	f	DOCK8	Non sense Y1875X	EBV, Candida, Cryptosporidium	likely
P73	Alsum Z, Hawwari A et al. (2013)		F3P1	f	DOCK8	Non sense Y1875X	HCMV, EBV	likely
P74	Alsum Z, Hawwari A et al. (2013)		F5P1	m	DOCK8	Non sense S1711X	Fungi, HBV, HCV, HCMV, EBV	likely
P75	Alsum Z, Hawwari A et al. (2013)		F6P1	f	DOCK8	Large deletion	HCMV, EBV, Cryptosporidium, HSV	likely
P76	Alsum Z, Hawwari A et al. (2013)		F7P2	m	DOCK8	presumed large deletion, based on sibling	HCMV, EBV, Cryptosporidium	possible
P77	Cavkaytar O, Cagdas Ayvaz D et al. (2013)		7y old girl	f	DOCK8	homozygous mutation was established by sequence analysis. A large deletion was found in DOCK8 gene between exons 1 to 9	Candida, A. flavus, M. catarrhalis	possible
P78	Daschkey S, Bienemann K et al. (2016)		1	f	FAAP24	homozygous c.C635T (exon 5) p.T212M	EBV	likely
P79	Daschkey S, Bienemann K et al. (2016)		2	m	FAAP24	homozygous c.C635T (exon 5) p.T212M	EBV	likely
P80	Colobran R, Alvarez de la Campa E et al. (2016)		case 3	m	FOXP3	X-linked c.1099T>G p.Phe367Val	Klebsiella	likely
P81	Morales M, Bakshi S et al. (1998)		Case1	m	FOXP3	(1–7G>T)leading to a stop signal at codon 61 of the normal exon 1	Klebsiella	possible
P82	Morales M, Bakshi S et al. (1998)		Case2	m	FOXP3	the predicted mutation (maternal) heterozygous form (S390N), G1169A	P. aeruginosa	likely
P83	Xavier-da-Silva MM, Moreira-Filho CA et al. (2015)	Myers AK, Perroni L et al. (2006)	4; case 1 in Myers	m	FOXP3	c.1-7G>T	K. pneumoniae	likely
P84	Xavier-da-Silva MM, Moreira-Filho CA et al. (2015)	Costa-Carvalho BT, De Moraes-Pinto MI et al. (2008)	6; BBP in Costa-Carvalho	m	FOXP3	g.13310C>G c.1045-3C>G	S. aureus, K. pneumoniae, P. aeruginosa, CoNS, Enterobacter	likely
P85	Xavier-da-Silva MM, Moreira-Filho CA et al. (2015)	Levy-Lahad E & Wildin RS (2001)	Patient 3 in both sources	m	FOXP3	c.1189C>T	P. carinii	likely
P86	Myers AK, Perroni L et al. (2006)		case 2	m	FOXP3	sequence alteration, G1169A was established in heterozygous form (S390N)	P. aeruginosa	likely
P87	Spinner MA, Ker JP et al. (2016)		A black woman	f	GATA2	frameshift mutation in intron 4 (c.87112_3insT)	HSV, Blastomyces	likely
P88	Spinner MA, Sanchez LA et al. (2014)		1.II.5‖	f	GATA2	1192C.T R398W	HPV, VZV, MAC, Aspergillus	possible
P89	Spinner MA, Sanchez LA et al. (2014)		12.I.1	m	GATA2	1083_1094del12 R361del4	HPV, HSV, HCV, M. kansasii, Candida	possible
P90	Spinner MA, Sanchez LA et al. (2014)		19.II.1	m	GATA2	1061C.T T354M	EBV, M. chelonae	possible
P91	Spinner MA, Sanchez LA et al. (2014)		22.I.1	f	GATA2	941_951dup A318fsX12	HPV, M. kansasii	possible
P92	Spinner MA, Sanchez LA et al. (2014)		23.I.3	m	GATA2	Uniallelic expression: undefined mutation with reduced or absent transcription from 1 allele by cDNA analysis	MAC	possible

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P93	Spinner MA, Sanchez LA et al. (2014)		26.I.1	f	GATA2	302delG G101AfsX16	HSV, HCMV	possible
P94	Robertson N, Engelhardt KR et al. (2015)		Patient 1	f	ICOS	a homozygous 10 base-pair deletion in Exon 2 (p.F108YfsX118)	NoV, HAdV, Cryptosporidium, HHV6	likely
P95	Sologuren I, Boisson-Dupuis S et al. (2011)		IV.1	f	IFNGR1	homozygous V63G mutation	MAC	possible
P96	Bukhari E, Alaklobi F et al. (2016)		5	f	IFNGR2	homozygous mutation,Y235x	BCG	likely
P97	Kilic SS, van Wengen A et al. (2012)		boy	m	IFNGR2	novel homozygous mutation, r.679G > A resulting in a G227R substitution	BCG	likely
P98	Toyoda H, Ido M et al. (2010)		Patient	m	IFNGR2	homozygous deletion 949delTG	MAC	possible
P99	Nielsen C, Jakobsen MA et al. (2014)		Patient	f	IKBKB	a nonsense mutation (c.814C>T) in the IKBKB gene encoding IKKβ (R272X, numbering according to NM_001556.2) situated on chromosome 8p11 within a large 50 Mb region of homozygosity	Enterobacter, M. bovis	likely
P100	Huppmann AR, Leiding JW et al. (2015)		7	m	IKBKG	c.944A.C E315A	MAC, S. aureus, K. oxytoca, S. maltophilia, S. viridans, C. lusitaniae	likely
P101	Huppmann AR, Leiding JW et al. (2015)		8	?	IKBKG	c.944A.C p.E315A	MAC	likely
P102	Huppmann AR, Leiding JW et al. (2015)		9	?	IKBKG	c.944A.C p.E315A	MAC, P. aeruginosa, H. influenzae	likely
P103	Huppmann AR, Leiding JW et al. (2015)		10	?	IKBKG	c.991del9 p.E331del3	S. pneumoniae, A. fumigatus, E. coli, Candida	likely
P104	Huppmann AR, Leiding JW et al. (2015)		13	m	IKBKG	c.1249T.C p.C417R	E. faecium, P. aeruginosa, Candida, C. glabrata	likely
P105	Mansour S, Woffendin H et al. (2001)		IP85	m	IKBKG	c.1259A>G p.X420W	HAdV, Mycobacterium	likely
P106	Niehues T, Reichenbach J et al. (2004)		Index case	m	IKBKG	hemizygous mutation (110-111insC) in exon 2	HSV	likely
P107	Orange JS, Jain A et al. (2004)		Patient 6	m	IKBKG	1167 insC	MAC	likely
P108	Orange JS, Jain A et al. (2004)		Patient 7	m	IKBKG	1167 insC	MAC, P. carinii	likely
P109	Ørstavik KH, Kristiansen M et al. (2006)		II-7	m	IKBKG	Exon 6 ISV6 + 5G>A (1027 + 5G>A)	P. carinii	likely
P110	Ørstavik KH, Kristiansen M et al. (2006)		III-7	m	IKBKG	exon 6 IVS6 + 5G>A (1027 + 5G>A)	Enterococcus, E. coli	possible
P111	Pannicke U, Baumann B et al. (2013)		Patient 1	f	IKBKG	homozygous duplication c.1292dupG in exon 13	MAC	likely
P112	Pannicke U, Baumann B et al. (2013)		Patient 2	f	IKBKG	homozygous duplication c.1292dupG in exon 13	L. monocytogenes	likely
P113	Ricci S, Romano F et al. (2017)		Patient	m	IKBKG	novel missense mutation c.1238A>G (p.H413R) within Exon 10	P. aeruginosa	likely
P114	Picard C, Fieschi C et al. (2002)		F.II.5	f	IL12B	g.315_316insA	M. chelonae, Salmonella B	likely
P115	Picard C, Von Bernuth H et al. (2010)		E.II.2	f	IL12B	g.315_316insA	BCG	likely

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P116	de Souza TL, Fernandes RCSC et al. (2017)		Case 1	m	IL12RB1	Trp7Ter	BCG	likely
P117	Pedraza-Sanchez S, Herrera-Barrios MT et al. (2010)		(P1)	f	IL12RB1	homozygous point mutation 1791+2 T>G	BCG, Candida	likely
P118	Pedraza-Sanchez S, Herrera-Barrios MT et al. (2010)		(P2)	m	IL12RB1	homozygous point mutation 1791+2 T>G	BCG	likely
P119	Fellmann F, Angelini F et al. (2016)		II.1	f	IL17RA, ADA2 (CECR1), XKR3	chromosome 22: homozygous deletion of 1790689186-1798389484	P. aeruginosa, Candida	likely
P120	Akar HH, Patiroglu T et al. (2016)	Patiroglu T, Akar HH et al. (2014)	P36	m	IL2RG	mutation in exon 5 (c.595-1G>T)	P. aeruginosa	possible
P121	Huang LH, Shyur SD et al. (2006)		8-month-old boy	m	IL2RG	c.407G>C p.R136P	BCG, P. aeruginosa	likely
P122	Lee WI, Chen CC et al. (2017)		SCID3-IL2RG	m	IL2RG	c.865 C>T p.Arg289Stop	Salmonella	likely
P123	Lee WI, Chen CC et al. (2017)		SCID4-IL2RG	m	IL2RG	c.854 G>A, skip exon 6	HCMV	likely
P124	Moya-Quiles MR, Bernardo-Pisa MV et al. (2014)		Boy	m	IL2RG	hemizygous mutation in exon 1, the mutation c.2T>C	HCMV	likely
P125	Okuno Y, Hoshino A et al. (2015)		Patient	m	IL2RG	p.P58T missense mutation	Aspergillus	likely
P126	Tsuji Y, Imai K et al. (2006)		Pat 2	m	IL2RG	Confirmed by mutational analysis	HCMV	likely
P127	Tsuji Y, Imai K et al. (2006)		Pat 3	m	IL2RG	Confirmed by mutational analysis	EBV	likely
P128	Tsuji Y, Imai K et al. (2006)		Pat 4	m	IL2RG	Confirmed by mutational analysis	CoNS	likely
P129	Takada H, Ishimura M et al. (2016)		1	?	IRAK4	homozygous c.123_124insA	S. pneumoniae	likely
P130	Takada H, Ishimura M et al. (2016)		5	?	IRAK4	homozygous c.123_124insA	S. pneumoniae	possible
P131	Takada H, Ishimura M et al. (2016)		6	?	IRAK4	homozygous c.123_124insA	S. pneumoniae	possible
P132	Takada H, Ishimura M et al. (2016)		7	?	IRAK4	homozygous c.123_124insA	P. aeruginosa	possible
P133	Takada H, Ishimura M et al. (2016)		9	?	IRAK4	homozygous c.123_124insA	S. pneumoniae	possible
P134	Strickler A, Gallo S et al. (2015)		Case	f	ITGB2	homozygous mutation c.1835G>T; p.C612F	E. faecium, K. pneumoniae, S. maltophilia	likely
P135	Zheng F, Li J et al. (2016)		Pt6	f	ITK	PRF1, UNC13D, ITK: Except ITK gene, gene mutations were identified as non-sense mutations. ITK: c.985+75G>A (at position chr5:156667232)	EBV	possible
P136	Zheng F, Li J et al. (2016)		Pt8	m	ITK	PRF1, UNC13D, STX11, STXBP2, XIAP, ITK: Except ITK gene, gene mutations were identified as non-sense mutations, mostly SNP. ITK: c.985+75G>A (at position chr5:156667232)	EBV	possible
P137	Kostel Bal S, Haskologlu S et al. (2017)	Serwas NK, Kansu A et al. (2015)	Pat 1; index in Serwas	f	LRBA	c.A8470C; c.T8471C; p.Ile2824Pr	Acinetobacter, Enterococcus, S. marcescens, C. krusei	likely
P138	Kaya Z, Ehl S et al. (2011)		second child	m	LYST	c.5506C>T, (p.Arg1836Stop) in exon 18	H1N1	possible
P139	Li FY, Chaigne-Delalande B et al. (2014)		B.1	m	MAGT1	g.29684C>T c.409C>T p.Arg137' ;	EBV	possible
P140	Li FY, Chaigne-Delalande B et al. (2014)		F.1	m	MAGT1	g.46604G.T c.859_997del139 p.Asn287*fs*1 ;	S. aureus	likely

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P141	Ben-Farhat K, Ben-Mustapha I et al. (2016)		P4	f	NCF2	c.257+2 T>C, predicted to affect RNA splicing	TB, Aspergillus	likely
P142	Ben-Farhat K, Ben-Mustapha I et al. (2016)		P6	f	NCF2	c.257+2 T>C, predicted to affect RNA splicing	Aspergillus	likely
P143	Boisson B, Puel A et al. (2017)	Moriya K, Sasahara Y et al. (2018)	P11	m	NFKBIA	S32R	S. aureus, Candida	likely
P144	Boisson B, Puel A et al. (2017)	Moriya K, Sasahara Y et al. (2018)	P12	m	NFKBIA	S32N	P. aeruginosa	likely
P145	Boisson B, Puel A et al. (2017)		P4	m	NFKBIA	E14X	GNB	likely
P146	Boisson B, Puel A et al. (2017)		P7	m	NFKBIA	M37K	E. faecium, A. lwoffii	likely
P147	Boisson B, Puel A et al. (2017)		P8	f	NFKBIA	M37R	K. pneumoniae, C. parapsilosis, S. maltophilia, Candida	likely
P148	Lundin KE, Hamasy A et al. (2015)		ND	?	PGM3	Ile322Thr	S. aureus	likely
P149	Elkaim E, Neven B et al. (2016)		10	m	PIK3R1	2-nt deletion at the splice donor site (GRCh38; NM181523.2; C.1425 12,3 position; TG deletion)	C. jejuni, Sal. ser. Typhimurium, C. difficile	likely
P150	Aytekin C, Dogu F et al. (2010)		1	f	PNP	c.G249A p.A117T	A. fumigatus	likely
P151	Aytekin C, Dogu F et al. (2010)		2	f	PNP	c.G249A p.A117T	TB	likely
P152	Gupta K, Rawat A et al. (2018)		1	m	PNP	c.244C>T; p.Q82X	HCMV, K. pneumoniae	possible
P153	Barmettler S, Nowak RJ et al. (2016)		index	f	PRF1	homozygous mutation, p.T450M	EBV, Metapneumovirus	possible
P154	Del Giudice E, Savoldi G et al. (2003)		index	m	PRF1	Allele A c.C694T p.Arg232Cys; Allele B carried an insertion of the TG dinucleotide at position 1191, resulting in a frameshift at His398, with premature termination at codon 420.	EBV	possible
P155	Iwatani S, Uemura K et al. (2014)		Our patient	m	PRF1	c.1A > G and c.1090_1091delCT	P. aeruginosa	likely
P156	Zheng F, Li J et al. (2016)		Pt4	m	PRF1	non-sesnse mutation, not further indicated	EBV	possible
P157	Szczawinska-Poplonyk A, Kycler Z et al. (2011)		Patient	f	RAB27A	confirmed by Rab27a gene sequencing, which identified a heterozygous mutation	EBV	possible
P158	Alkhairy OK, Rezaei N et al. (2015)		proband	f	RAC2	homozygous p.W56X	S. pyogenes	possible
P159	Akar HH, Patiroglu T et al. (2016)		P26	f	RAG1	c.1229 G>A, p.Arg410Gln	HCMV	possible
P160	Akar HH, Patiroglu T et al. (2016)		P28	f	RAG1	c.2209C>T, p.Arg737Cys	BCG	likely
P161	Avila EM, Uzel G et al. (2010)		1	f	RAG1	R396C (1186C>T) and R975Q (975G>A)	Candida, MAC	likely
P162	Buchbinder D, Baker R et al. (2015)		Case 2	f	RAG1	c.1566G>T, p.W522C and c.2689C>T, p. R897X. (Additionally heterozygous variant c.191G>T, p.P21R in TNFRSF13C)	NoV, Aspergillus	likely
P163	Dhingra N, Yadav SP et al. (2014)		case	m	RAG1	homozygous c:2881T>C; p:I794T	C. indologenes	likely
P164	Lynch MK, Jones CH et al. (2006)			?	RAG1	R396c C256	GNB	likely
P165	Martinez-Martinez L, Vazquez-Ortiz M et al. (2012)		Pat1	m	RAG1	c.631delT	P. jirovecii	likely

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P166	Martinez-Martinez L, Vazquez-Ortiz M et al. (2012)		Pat3	m	RAG1	c.631delT	CoNS	likely
P167	Pasic S, Djuricic S et al. (2009)		Patient 2	f	RAG1	homozygous dinucleotide deletion g.368–369delAA	G. lamblia	likely
P168	Pasic S, Djuricic S et al. (2009)		Patient 3	m	RAG1	homozygous dinucleotide deletion g.368–369delAA	HCMV, Sal. ser. Enteritidis	likely
P169	Schröder C, Baerlecken NT et al. (2017)		Male	m	RAG1	c.1123CNG, p.H375D and c.1430delC, p.F478Sfs*14, c.1420CNT, p.R474C, rs199474678	JCPyV	likely
P170	Dalal I, Tabori U et al. (2005)		3	f	RAG2	homozygous c.1305G>T p.Gly35Val	HPIV-3	likely
P171	Dutmer CM, Asturias EJ et al. (2015)		case	f	RAG2	heterozygous R73H and presumably de novo P180H	VZV Oka, Mumps Jeryll Lynn, Rubella RA27/3	likely
P172	Gupta K, Rawat A et al. (2018)		2	m	RAG2	c.1247 C>T p.W416L	E. cloacae, HCMV	likely
P173	Gupta K, Rawat A et al. (2018)		5	m	RAG2	c.921G>A; p.W307X	HCMV, Aspergillus	likely
P174	Sadeghi-Shabestari M, Vesal S et al. (2009)		first child	f	RAG2	homozygous c.1782C>A (p.S194X) and c.1784T>G (p.Y195D)	BCG	likely
P175	Sadeghi-Shabestari M, Vesal S et al. (2009)		second child	m	RAG2	homozygous c.1782C>A (p.S194X) and c.1784T>G (p.Y195D)	BCG	likely
P176	Horn J, Schlesier M et al. (2010)		28-year old woman	f	RMRP	g.68_69delinsTT and g.76C>T	S. pneumoniae, M. catarrhalis, H. influenzae	likely
P177	Hanna S, Béziat V et al. (2015)	Etzioni A, Eidenschenk C et al. (2005)	23-month-old girl in both sources	f	RTEL1	c.3791G>A; p.R1264H	VZV	likely
P178	Brandau O, Schuster V et al. (1999)		3a	m	SH2D1A	c.T599A p.Y100X	EBV	likely
P179	Brandau O, Schuster V et al. (1999)		8a	m	SH2D1A	c.C601T p.P101L	EBV	likely
P180	Morra M, Silander O et al. (2001)		B.C.	m	SH2D1A	(R55X)	EBV	possible
P181	Morra M, Silander O et al. (2001)		C.L.	m	SH2D1A	(R55X)	EBV, Aspergillus	likely
P182	Nistala K, Gilmour KC et al. (2001)		1	m	SH2D1A	G39V	EBV	possible
P183	Overwater E, Smulders Y et al. (2014)		Patient	f	SH2D1A	missense mutation n c.131G>A	EBV	likely
P184	Schuster V, Hellebrand H et al. (2000)		boy	m	SH2D1A	(Y100X mutation was found in mother and two further obligate carriers)	EBV	likely
P185	Sun J, Ying W et al. (2013)		Patient 3	m	SH2D1A	substitution c.138-2A>G Splice acceptor defect, Exon skipping	EBV	possible
P186	Sun J, Ying W et al. (2013)		Patient 4	m	SH2D1A	substitution c.161A>G P.Y54C Missense defect	EBV	possible
P187	Sharfe N, Nahum A et al. (2014)		Pat. 2	f	STAT1	heterozygous de novo T385M G>A substitution (c1154T)	HCMV	likely
P188	Sharfe N, Nahum A et al. (2014)		Pat. 3	m	STAT1	heterozygous de novo T385M G>A substitution (c1154T)	EBV	likely
P189	Sharfe N, Nahum A et al. (2014)		Pat. 4	f	STAT1	de novo I294T	JaCaV	likely
P190	Wessell KR, Tcheurekdjian H & Hostoffer R (2016)		1	m	STAT1	DNA binding Thr385Met mutation	JCPyV	likely

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P191	Chandesris MO, Melki I et al. (2012)		P19	f	STAT3	p.S611G	S. pneumoniae	likely
P192	Chandesris MO, Melki I et al. (2012)		P45	f	STAT3	p.Vdel463	S. pneumoniae	likely
P193	Wu J, Chen J et al. (2017)		P14	m	STAT3	Exon 22, c. 2123C>G	P. jirovecii	possible
P194	Giannelou A, Wang H et al. (2018)		7	f	TRNT1	heterozygous compound mutations: c.329C>T p.Thr110Ile; c.383A>G p.Asp128Gly	S. aureus	likely
P195	Kinnear C, Glanzmann B et al. (2017)		index patient	m	TTC37	homozygous missense mutation c. 4507C> T (rs200067423) in exon 42 of TTC37 (NM_014639) which results in the substitution of an arginine with a cysteine atamino acid 1503 (p.R1503C)	HCMV	possible
P196	Kinnear C, Glanzmann B et al. (2017)		sibling	m	TTC37	homozygous missense c 4507C> T mutation (rs200067423)	Klebsiella, Enterococcus	possible
P197	Lee WI, Huang JL et al. (2016)		Taiwanese 2	f	TTC37	c.3507 G>T, p.Y1169*; c.Ins 3724A, p.InsA1143S Fs*3	HRSV, S. aureus, K. pneumoniae	likely
P198	Park M, Yun YJ et al. (2015)		Case report	f	UNC13D	17q25	Rotavirus	possible
P199	Cannioto Z, Berti I et al. (2009)		14	m	WAS	not indicated	P. carinii	likely
P200	Folwaczny C, Ruelfs C et al. (2002)		30-year-old man	m	WAS	c.95C>T	JCPyV	likely
P201	Hacein-Bey Abina S, Gaspar HB et al. (2015)		3	m	WAS	c.628delT p.S210HfsX51	VZV, HSV, HCMV, EBV, Aspergillus	likely
P202	Huang KY, Lai MW et al. (2008)		The patient	m	WAS	large deletion in the WAS (WASP) gene that encompassed the promoter, exon 1 and exon 2	HCMV, MRSA	likely
P203	Lee WI, Chen CC et al. (2017)		WAS1	m	WAS	Del promoter, exon 1 and 2	S. aureus	likely
P204	Lee WI, Huang JL et al. (2010)		3	?	WAS	Exon 1, missense, 91 G>A, Glu 31 Lys	S. pneumoniae, Aeromonas	likely
P205	Lee WI, Huang JL et al. (2010)		6	?	WAS	Exon 1, nonsense, 121 C>T, Arg 41 stop	HCMV, S. aureus	likely
P206	Lee WI, Huang JL et al. (2010)		7	?	WAS	Exon 1, splice, IVS 1 (-1) G>C, Del 43 aa and Del exon 2	EBV	possible
P207	Lee WI, Huang JL et al. (2010)		8	?	WAS	huge deletion including promoter, exon 1 and exon 2	S. aureus, S. agalactiae	likely
P208	Lee WI, Kuo ML et al. (2005)		23	m	WAS	huge deletion, involving promoter, exon 1 and exon 2	Salmonella B, S. aureus, HCMV, HCV	likely
P209	Suri D, Singh S et al. (2012)		3	?	WAS	point mutation, missense mutation, exon 1, c.91G>A, p.Glu31Lys	Candida, S. aureus, VZV	likely
P210	Suri D, Singh S et al. (2012)		4	?	WAS	point mutation, nonsense mutation, exon 1, c.37C>T, p.Arg13*	S. aureus	possible
P211	Tsuji Y, Imai K et al. (2006)		Pat 7	m	WAS	Confirmed by mutationial analysis	HCMV	likely
P212	Tsuji Y, Imai K et al. (2006)		Pat 8	m	WAS	Confirmed by mutationial analysis	EBV	likely
P213	Brochstein JA, Gillio AP et al. (1991)		UPN 858	m	WAS?	clinical diagnosis on the basis of thrombocytopenia, small platelet size, and variable degrees of eczema and immunodeficiency	HCMV	likely
P214	Brochstein JA, Gillio AP et al. (1991)		UPN 870	m	WAS?	clinical diagnosis on the basis of thrombocytopenia, small platelet size, and variable degrees of eczema and immunodeficiency	Candida	likely
P215	Brochstein JA, Gillio AP et al. (1991)		UPN 914	?	WAS?	clinical diagnosis on the basis of thrombocytopenia, small platelet size, and variable degrees of eczema and immunodeficiency	EBV	likely
P216	Brochstein JA, Gillio AP et al. (1991)		UPN 926	?	WAS?	clinical diagnosis on the basis of thrombocytopenia, small platelet size, and variable degrees of eczema and immunodeficiency	EBV	likely

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link
P217	Heidelberger KP & LeGolvan DP (1974)		the patient	m	WAS?	clinical diagnosis	S. aureus, P. aeruginosa	likely
P218	Horwich AL, Seashore MR & Dwyer JM (1984)		Present report 34	m	WAS?	clinical diagnosis	S. pneumoniae	likely
P219	Ilowite NT, Fligner CL & Ochs HD (1986)		The boy	m	WAS?	clinical diagnosis	FLUBV, Nocardia	likely
P220	Standen GR, Orchard JA & Hutton RD (1990)		Patient DC	m	WAS?	clinical diagnosis	S. pneumoniae	likely
P221	Kuhns DB, Fink DL et al. (2016)		II.2.2.	f	WDR1?	Because no DNA from her was recoverable, her genotype was inferred from her parents and sibling. She is presumed to have been compound heterozygous for delK7 and V424M.	VZV	likely
P222	Sun J, Ying W et al. (2013)		Patient 2	m	XIAP	substitution c.1100A>G P.D367G splice site mutation	EBV	possible
P223	Akar HH, Patiroglu T et al. (2016)		P31	m	ZAP70	c.1193C>T, p.Ile398Ser	HSV, HCMV	possible
P224	De Greef JC, Wang J et al. (2011)	Hagleitner MM, Lankester A et al. (2008)	P2, 11 in Hagleitner	f	ZBTB24	homozygous c.47C>G p.Ser16X	P. jirovecii	likely
P225	De Greef JC, Wang J et al. (2011)	Hagleitner MM, Lankester A et al. (2008)	P3, 17 in Hagleitner	f	ZBTB24	homozygous c.958C>T p.Arg320X	P. aeruginosa	likely

11.8. Appendix H – Table 10: Extracted cases with issues

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link	Issue
Q1	Alsum Z, Hawwari A et al. (2013)		F8P1	f	? (autosomal recessive Hyper IgE syndrome)	no mutation found in TYK2 or STAT3 but three copies of the region 440829 to 433626 (7.2 kb) within the DOCK8 gene. Could not be confirmed in sequencing. Protein expression not analysed.	HCMV, HSV	likely	is there a clear gene candidate for HIES? (TYK2 and STAT3 was wild-type, DOCK8 may have a some duplication, but this could not be confirmed in sequencing)
Q2	Baumal CR, Levin AV & Read SE (1999)		6	f	? (SCID)	Clinical diagnosis, no mutation analysis	HCMV	possible	Is there a gene candidate for this this patient with SCID?
Q3	Baumal CR, Levin AV & Read SE (1999)		4	m	? (SCID)	Clinical diagnosis, no mutation analysis	HCMV	likely	Is there a gene candidate for this this patient with SCID?
Q4	Brandau O, Schuster V et al. (1999)		5a	m	? (X-linked lymphoproliferative syndrome)	no mutation in SH2D1A or TNM1	VZV	likely	Is there a clear gene candidate for X-linked lymphoproliferative syndrome (not SH2D1A or TNM1)
Q5	Doncker AV, Balabanian K et al. (2011)		Patient 2	f	? (severe defect in CXCL12-promoted internalization but no myelokathexis in bone marrow biospsies)	Both alleles of CXCR4 were shown to be wild type	MAC, Mucormycotina	likely	Is there a clear gene candidate for this patient? CXCR4 was wild type...
Q6	Gupta K, Rawat A et al. (2018)		8	?	? (chronic granulomatous disease with extensive haemophagocytosis)	no mutations in CYBA, NCF2, NCF4 and no GT deletion in NCF1 gene. NCF1 gene not sequenced in its entirety	Aspergillus	possible	Is there a gene candidate? Clinical diagnosis is chronic granulomatous disease with extensive
Q7	Gupta K, Rawat A et al. (2018)		6	m	? (SCID)	no mutation found in IL2RG, RAG1 and RAG2	Aspergillus	likely	Is there a gene candidate for this patient with SCID?
Q8	Gupta K, Rawat A et al. (2018)		4	m	? (SCID)	no mutation found in IL2RG	HCMV, P. jirovecii	likely	Is there a gene candidate for this patient with SCID?
Q9	Gupta K, Rawat A et al. (2018)		3	m	? (SCID)	no mutational analysis done	Mucorales, K. pneumoniae	likely	Is there a gene candidate for this patient with SCID?
Q10	Kim HY, Kim YM & Park HJ (2017)		case report	f	? (CHARGE syndrome with SCID (T-, B+, NK-))	No deletion or duplication of the CHD7 gene was found	BCG	likely	Is there a clear gene candidate that could be suspected for SCID with CHARGE syndrome in this patient?
Q11	Lee WI, Huang JL, Lin SJ et al. (2011)		5	m	? (autosomal dominant Hyper IgE syndrome)	no mutation found in STAT3	P. mirabilis	likely	is there a clear gene candidate for HIES? (STAT3 is wild-type)
Q12	Lee WI, Huang JL, Lin SJ et al. (2011)		6	f	? (autosomal dominant Hyper IgE syndrome)	no mutation found in STAT3	S. aureus	likely	is there a clear gene candidate for HIES? (STAT3 is wild-type)
Q13	Tsuji Y, Imai K et al. (2006)		Pat 5	m	? (SCID T-B-NK+)	no mutational analysis done	CoNS, HCMV	possible	Is there a gene candidate for this patient with SCID?
Q14	Wolska-Kusnierz B, Bajer A et al. (2007)		Patient 3	m	? (idiopathic CD4 lymphopenia)	no mutation in SAP gene [which gene is that?]. Normal CD40 ligand expression	C. hominis, intestinal perforation?	possible	Is there a clear gene candidate for idiopathic CD4 lymphopenia?
Q15	Yang YL, Lu MY et al. (2005)		10 (LAD)	f	? (Leukocyte adhesion deficiency)	Clinical diagnosis of Leukocyte adhesion deficiency (LAD)	Candida	likely	Is there a gene candidate for this this patient with Leukocyte adhesion deficiency (LAD)?
Q16	Yang YL, Lu MY et al. (2005)		4 (SCID)	f	? (SCID T-B-)	Clinical diagnosis of SCID. No clear gene candidate	P. aeruginosa	likely	Is there a gene candidate for this this patient with SCID?
Q17	Lainka E, Hershfield MS et al. (2005)		10-month-old girl	f	ADA	Homozygosity for missense mutation, Val129Met in exon 5	HCMV, other viral infection?	likely	Which viral pathogen is responsible for the overwhelming infection post-HSCT?

#	Reference	Cited from	Patient	Gender	Gene	Mutation	Infectious agent	Causal link	Issue
Q18	Gupta K, Rawat A et al. (2018)		9	m	ATM?	no mutational analysis done	Aspergillus	likely	Is clinical diagnosis of AT sufficient to suspect ATM gene? (Patient died of Aspergillus pneumonia combined with Hodgkin's lymphoma)
Q19	Cabral-Marques O, Klaver S et al. (2014)	Danielian S, Oleastro M et al. (2007)	20; 2a in Danielian	?	CD40LG	FS del c.500delG p.M148X153	G. lamblia	possible	Is there any link between G. lamblia infection and progressive panencephalitis? Ocular damage has been described previously, but not with cerebral involvement... doi.org/10.3748/wjg.v19.i47.8974
Q20	Cabral-Marques O, Klaver S et al. (2014)		32	?	CD40LG	c.159C>T p.Q35X	P. jirovecii	possible	Is there any link between P. jirovecii and fatal encephalopathy?
Q21	Lee WI, Huang JL et al. (2013)	Lin SC, Shyur SD et al. (2006)	B1; case 1 in Lin	m	CD40LG	missense, T 526->A exon 5 Tyr 169 Asn TNF-H	S. aureus, Cryptococcus, Candida, renal carcinoma?	unlikely	Is there a possible link between infection and renal cell carcinoma?
Q22	Wu J, Wang WF et al. (2017)		P23	m	CYBB	Deletion Exon 10, c.1313 1314, p.K438IfsX63	B. cepacia	likely	Is B. cepacia the pathogen responsible for fatal septicopyemia? Question sent to tongxinc@yahoo.com
Q23	Wu J, Wang WF et al. (2017)		P29	m	CYBB	Nonsense Exon 8, c.868C>T, p.R290X	BCG	likely	Is B. cepacia the pathogen responsible for fatal septicopyemia? Question sent to tongxinc@yahoo.com
Q24	Lee PP, Woodbine L et al. (2013)	Peake J, Waugh A et al. (1999)	2; boy in Peake	m	DCLRE1C	Compound heterozygous p.Leu70del, p.Gly126Asp. Most details in Evans et al. 10.1093/hmg/ddl050	Candida, ?transplant-related complications?	possible	Need to contact author about transplant-related complications (which pathogen?)
Q25	Hagleitner MM, Lankester A et al. (2008)		8	m	DNMT3B	Ins1bp/D737het	Candida	possible	Respiratory failure due to candida seems unlikely, clarification requested from c.weemaes@cukz.umcn.nl
Q26	Alsum Z, Hawwari A et al. (2013)		F3P4	f	DOCK8	Non sense Y1875X	Candida, Aspergillus, fatal pneumonia and sepsis??	likely	Which pathogen is responsible for pneumonia and sepsis?
Q27	Spinner MA, Sanchez LA et al. (2014)		7.I.1	f	GATA2	Uniallelic expression: undefined mutation with reduced or absent transcription from 1 allele by cDNA analysis	M. kansasii, HPV	possible	Did Mycobacterium and HPV infection contribute significantly to this fatality at old age?
Q28	Huppmann AR, Leiding JW et al. (2015)		5	?	IKBKG	c.936C.G p.F312L	MAC, S. pneumoniae, Candida, A. xylosoxidans, HCMV, EBV	possible	Is there any link between the mentioned infections and thrombocytopenia-linked GI haemorrhage?
Q29	Kostel Bal S, Haskologlu S et al. (2017)		Pat 3	m	LRBA	c.3196del, c.7976G > C, pAsp1053fs, p.Ser2659* (compound heterozygous)	EBV, HCoV-OC43, S. aureus, C. glabrata	possible	Which role did the various pathogens play? Clarification requested form aydani@medicine.ankara.edu.tr
Q30	Akar HH, Patiroglu T et al. (2016)		P40	m	MAGT1	c.555dup, p.Tyr186Ilefs*2	HCMV, EBV	possible	Is there any link between EBV or CMV infection and intracranial haemorrhage post-HSCT
Q31	Burda P, Kuster A et al. (2015)		4	f	MTHFD1	from father: c.146C>T, p.Ser49Phe and from mother: c.673G > T, p.Glu225*	Candida	possible	Can we use this case? No cultures were obtained, therefore no pathogens were identified.
Q32	Boisson B, Puel A et al. (2017)	Janssen R, van Wengen A et al. (2004)	P2	m	NFKBIA	S32I	S. pyogenes, P. jirovecii, Candida, progressive tetraplegia and axial hypertonia?	unlikely	Is there any link between progressive tetraplegia and pathogens mentioned (Strep.A, P.jirovecii, CMC)?
Q33	Gerard LM, Barth D et al. (2012)		52-year old male	m	PRF1	c.1517C>T	EBV, Blastomyces, polymicrobial sepsis??	likely	Is this patient too old? How to report polymicrobial sepsis? EBV plays a role in reactivation of HLH, the combination with Blastomyces killed the patient in the end.
Q34	Khan TA, Iqbal A et al. (2017)		Patient	f	RAG1	novel missense mutation (c. 307C > T/p.H103Y)	C. violaceum, the fatal bugs are not indicated!?	likely	Died post-HSCT of which pathogens? Clarification requested from microbiologist63@yahoo.com
Q35	Faitelson Y, Bates A et al. (2014)		East Indian origin	f	STAT1	c.(1189A > G)];(=) in NM_007315.3 resulting in amino acid substitution p.(Asn397Asp);(=)(A)	HSV, EBV	possible	Is this a case of EBV- or HZV-triggered HLH?

12. Curriculum vitae

Surname, Given names:	Killian, Michael Paul Martin
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Education:

1996 - 1998	Berger-Höhe Schule, Wangen im Allgäu (D)
1998 - 2000	De Vrije School Den Haag (NL)
2000 - 2006	De Vrije School Den Haag (2000-2006), graduated in 2006 - “VWO”, Dutch matriculation for admission to University
2009 - 2011	Monash University, Melbourne (AUS), Bachelor of Nursing
2011 - 2012	Haute École de Santé – Fribourg (CH), Bachelor of Nursing
2014 - 2017	University of Fribourg (CH), Bachelor of Medicine
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13. Denial of Plagiarism Declaration (in German)

Masterarbeit

Ich erkläre ausdrücklich, dass es sich bei der von mir im Rahmen des Studiengangs *Humanmedizin* eingereichten schriftlichen Arbeit mit dem Titel

Fatal infections in primary immunodeficiencies - how to setup a systematic review

um eine von mir selbst und ohne unerlaubte Beihilfe sowie *in eigenen Worten* verfasste Masterarbeit* handelt.
Ich bestätige überdies, dass die Arbeit als Ganzes oder in Teilen weder bereits einmal zur Abgeltung anderer Studienleistungen an der Universität Zürich oder an einer anderen Universität oder Ausbildungseinrichtung eingereicht worden ist.

Verwendung von Quellen
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Ich bestätige mit meiner Unterschrift die Richtigkeit dieser Angaben.

Datum:

Name: Killian Vorname: Michael

Unterschrift:……………………………………..*nur auf Printversion erforderlich*

* Falls die Masterarbeit eine Publikation enthält, bei der ich Erst- oder Koautor/-in bin, wird meine eigene Arbeitsleistung im Begleittext detailliert und strukturiert beschrieben.