Universitätsklinikum
Carl Gustav Carus
DIE DRESDNER.

Schwere Ekzeme im Rahmen von Immundefekten

Dr. med. Julia Körholz
Kinderklinik und Poliklinik des Universitätsklinikums Dresden
21. Mai 2022

UniversitätsCentrum für Seltene Erkrankungen

Was sind Immundefekte mit Ekzem?

IEI + Ekzem

XL: **Wiskott Aldrich Sd or XL thrombocytopenia *WAS (LOF)***. Recurrent bacterial and viral infections; bloody diarrhea; eczema; lymphoma; autoimmune disease; IgA nephropathy; vasculitis. Small platelets; Decreased IgM. Low antibody to polysaccharides; often increased IgA and IgE. Nl Bc. Tc: Progressive decrease in numbers; Low Tc responses to anti-CD3.
Patients with XL-thrombocytopenia have later onset of complications and more favourable life expectancy but eventually develop similar complications as observed in WAS

IPEX, immune dysregulation, polyendocrinopathy, enteropathy X-linked. *FOXP3.* Autoimmune enteropathy, early onset diabetes, thyroiditis hemolytic anemia, thrombocytopenia, eczema, elevated IgE, IgA. Lack and/or impaired function of $CD4^+$ $CD25^+$ $FOXP3^+$ regulatory T cells (Tregs).

IIb. CID with associated or syndromic features

Hyper-IgE syndromes (HIES)

AD-HIES (Job sd). *STAT3,* AD LOF. Distinctive facial features (broad nasal bridge); bacterial infections (boils and pulmonary abscesses, pneumatoceles) due to *S. aureus, Aspergillus, Pneumocystis jirovecii*; eczema; mucocutaneous candidiasis; hyperextensible joints, osteoporosis and bone fractures, scoliosis, retention of primary teeth; aneurysm formation. IgE ↑↑; specific antibody production↓. Bc:Normal; reduced switched and non-switched memory Bc; BAFF expression ↑. Tc:Nl overall; Th-17 & T-follicular helper cells ↓

ZNF341 deficiency. *ZNF341.* AR. Phenocopy of AD-HIES: Mild facial dysmorphism, early onset eczema, MCC, bacterial skin infections, abscesses, recurrent bacterial respiratory infections (S. aureus), lung abscesses and pneumatoceles, hyperextensible joints, bone fractures and retention of primary teeth

Comel Netherton Sd; *SPINK5;* Congenital ichthyosis, bamboo hair,atopic diathesis; ↑ bacterial infections, failure to thrive. ↑ IgE and IgA; Other Ig: variably decreased. Bc: Switched and non-switched Bc are↓.

PGM3 deficiency. *PGM3.* Severe atopy; autoimmunity; skeletal anomalies: short stature, brachydactyly, dysmorphic facial features. Recurrent pneumonia, recurrent skin abscesses,bacterial and viral infections; cognitive impairment; delayed CNS myelination in some. Ig:Nl or elevated. Elevated IgE; eosinophilia. Reduced B and memory Bc. CD8 and CD4 Tc may be↓.

CID with early-onset asthma, eczema and food allergies, autoimmunity ID with atopic dermatitis (CADINS)*. *CARD11.* AD LOF. Variable atopy, cutaneous viral infections, recurrent respiratory infections, lymphoma. Eosinophilia, ↓Tc proliferation. Nl to low Bc.

ERBIN deficiency. *ERBB21P.*** Recurrent respiratory infections, susceptibility to S. aureus, eczema, hyperextensible joints, scoliosis, arterial dilatation in some. Moderately increased IgE; increased Treg.

IL6R deficiency*. *IL6R.* Recurrent pyogenic infections, cold abscesses, high circulating IL-6 Levels.

IL6ST deficiency*. *IL6ST.* Bacterial infections, boiles, eczema, pulmonary abscesses, pneumatoceles, bone fractures, scoliosis, retention of primary teeth, craniosynostosis. ↓B-cell memory.

Loes-Dietz syndrome, *TGFBR1, TGFBR2.* Recurrent respiratory infections, eczema, food allergies, hyperextensible joints, scoliosis, retention of primary teeths; aortic aneurisms.

Defects of Vitamin B12 and Folate Metabolism:

Megaloblastic anemia, Ig: decreased.

Transcobalamin 2 deficiency. *TCN2.* pancytopenia, if untreated for prolonged periods results in intellectual disability.

Deficiency causing hereditary folate malabsorbtion. *SLC46A1.* failure to thrive, if untreated for prolonged periods results in intellectual disability

Methylene-tetrahydrofolate dehydrogenase 1 deficiency *MTHFD1.* Recurrent bacterial infection, *Pneumocystis jirovecii; failure to* thrive; neutropenia; seizures, intellectual disability; folate-responsive ↓ Bc, ↓ antibody responses to conjugated polysaccharide antigens.

Anhidrotic Ectodermodysplasia with ID

Anhidrotic ectodermal dysplasia,various infections (bacteria, mycobacteria, viruses and fungi), colitis, variable defects of skin, hair and teeth.

NEMO deficiency. *IKBKG (NEMO).* XL, monocyte dysfunction. Ig decreased, some with elevated IgA, IgM, poor specific antibody responses, absent antibody to polysaccharide antigens. Bc: Nl, Low memory and isotype switched Bc. Tc: Nl/decreased, TCR activation impaired.

EDA-ID due to IKBA GOF mutation. *NFKBIA (IKBA).* AD Tc and monocyte dysfunction Decreased IgG and IgA, elevated IgM, poor specific antibody responses, absent antibody to polysaccharide antigens. Normal Bc numbers, impaired BCR activation, low memory and isotype switched Bc. Normal total Tc, TCR activation impaired.

EDA-ID due to IKBK GOF mutation* *IKB8.* AD. Low Tc. Bc: Nl number, poor function. Low Ig.

Others

Purine nucleoside phosphorylase deficiency. *PNP.* Autoimmune haemolytic anemia, neurological impairment. Hypouricemia. Ig : Nl/Low. Bc: Nl. Tc: Progressive decrease

Calcium Channel Defects. Autoimmunity, EDA, non-progressive myopathy. Ig and Bc: Nl. Tc: Normal, defective TCR mediated activation. **ORAI-1 deficiency*. *ORAI1* . *STIM1* deficiency*. *STIM1***

ID with multiple intestinal atresias. *TTC7A* . Bacterial (sepsis), fungal, viral infections, multiple intestinal atresias, often with intrauterine polyhydramnios and early demise, some with SCID phenotype. Markedly decreased IgG, IgM, IgA. Bc:Nl/low.Tc: Variable/absent, low TRECs (may present with SCID at birth)

Hepatic veno-occlusive disease with immunodeficiency (VODI). *SP110.* Hepatic veno-occlusive disease, *Pneumocystis jirovecii* pneumonia, CMV, candida, thrombocytopenia, hepatosplenomegaly, cerebrospinal leukodystrophy. Decreased IgG, IgA, IgM, absent germinal centers and tissue plasma cells. Decreased memory Bc . Decreased memory Tc.

STAT5b deficiency. *STAT5B.* AR. Growth-hormone insensitive dwarfism, dysmorphic features, eczema, lymphocytic interstitial pneumonitis, autoimmunity. Hypergammaglobulinemia, High IgE. ***AD DN:*** Growth failure and eczema only. High IgE.

BCL11B deficiency. *BCL11B.* AD. Congenital abnormalities: neonatal teeth, dysmorphic facies; absent corpus callosum; neurocognitive deficits. Tc : Low, poor proliferation.

Hennekam-lymphangiectasia-lymphedema syndrome*. *CCBE1, FAT4.* Lymphangiectasia and lymphedema with facial abnormalities and other dysmorphic features. Ig: decreased. Bc and Tc: Variable.

Bacterial infections, autoinflammation, amylopectinosis.Bc: Nl,decreased memory Bc.
HOIL1 deficiency. *RBCK1.* Poor Ab responses to polysaccharides. **HOIP deficiency*. *RNF31.*** Lymphangiectasia. Ig: decreased.

Vici syndrome. *EPG5.* Agenesis of the corpus callosum, cataracts, cardiomyopathy, skin hypopigmentation, intellectual disability, microcephaly, CMC. Ig: Decreased IgG2. Bc: Defective. Profound depletion of CD4+ cells.

Kabuki Sd. *KMT2D (MLL2):* AD. ***KDM6A:*** XL.
Typical facial abnormalities, cleft or high arched palate, skeletal abnormalities, short stature, intellectual disability, congenital heart defects, recurrent infections (otitis media, pneumonia) in 50% of patients. Autoimmunity may be present. Low IgA and occasionally low IgG.

Wiedemann-Steiner Sd, *KMT2A (MLL):* AD Respiratory infections; short stature; hypertelorism; hairy elbows; developmental delay, intellectual disability. Hypogammaglobulinemia, decreased memory Bc.

Immunodeficiency, developmental delay and hypohomocysteinemia, IMDDHH*. Activating de-novo mutations in *NFE2L2.* AD. Recurrent respiratory and skin infections, growth retardation, developmental delay; white matter cerebral lesions, decreased level of homocysteine; increased expression of stress response genes. Hypogammaglobulinemia. Bc: Decreased switched-memory Bc.

Tricho-Hepato-Enteric syndrome. *TTC37; SKIV2L*.* Respiratory infections, IUGR, wooly hair, early onset intractable diarrhea, liver cirrhosis, platelet abnormalities. Impaired IFNγ production, Hypogammaglobulinemia, low antibody responses. Bc: Variably low switched-memory Bc.

Bousfiha et *al., J Clin Immunol* 2020

IEI + erhöhtes IgE

Other PIDs with high serum IgE levels

Several other PIDs mainly from the CID category are characterized by high serum IgE levels and susceptibility to infections. The PIDs, including Wiskott–Aldrich syndrome, DOCK8 deficiency, PGM3 deficiency, and Omenn Syndrome, are all characterized by decreases in T-cell numbers and an impairment in T-cell proliferation. Causative genes of Omenn syndrome include Recombination-activating gene *(RAG)1, RAG2, IL2RG, IL7R, DNA ligase 4 (LIG4), DNA cross-link repair 1C (DCLRE1C), RNA component of mitochondrial RNA processing endoribonuclease (RMRP), adenosine deaminase (ADA), protein kinase, DNA-activated, catalytic (PRKDC).* The high serum IgE levels may result from weak TCR signaling insufficient to induce Treg cells, and/or an imbalance in the Th1/Th2 differentiation. Immune-dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome is caused by the LOF mutations in the *FOXP3* gene, is also one of the PID with high serum IgE levels. This indicates that the lack of regulatory T cells alone is sufficient to induce high serum IgE levels in the patient. It is necessary to exclude these disorders/genes to diagnose HIES.

Minegichi et *al., Allergol Int.* 2021

Wann muss ich an einen Immundefekt denken?

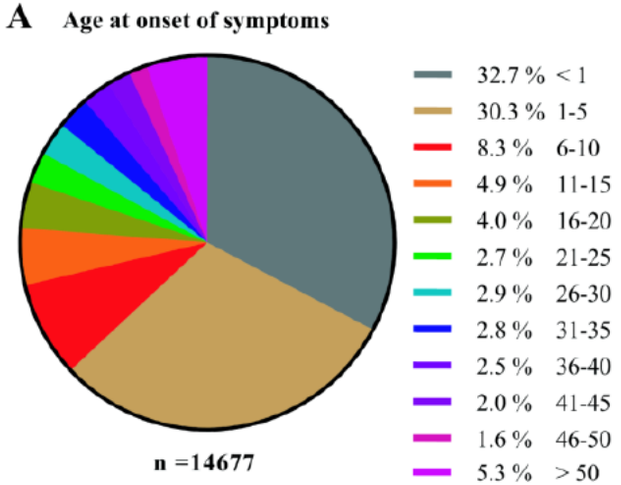


Table III: Presenting symptoms by age groups

	<1	1-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	46-50	>50	Total
Infections	74.3%	80.7%	81.1%	79.2%	86.3%	82.9%	86.7%	91.2%	88.3%	91.0%	88.5%	92.9%	11779
Immune dysregulation	18.1%	17.6%	23.6%	28.0%	24.8%	24.3%	20.6%	15.2%	20.5%	22.1%	16.1%	11.5%	2797
Malignancy	0.3%	0.6%	1.0%	1.2%	1.8%	1.3%	1.9%	1.3%	2.0%	2.5%	4.4%	2.2%	127
Syndromic	21.6%	15.9%	9.1%	7.2%	2.3%	4.1%	4.1%	1.5%	2.0%	1.1%	0.4%	1.1%	1938

Thalhammer et al. *JACI* 2021

AWMF-Register Nr.	112-001	Klasse:	S2k

Leitlinie

„Diagnostik auf Vorliegen eines primären Immundefekts“

- Abklärung von Infektionsanfälligkeit, Immundysregulation und weiteren Symptomen von primären Immundefekten –

- **ELVIS** (pathologische Infektanfälligkeit)
  - **E** – Erreger
  - **L** – Lokalisation
  - **V** – Verlauf
  - **I** – Intensität
  - **S** – Summe

https://www.horror-shop.com/p/elvis-presley-kostuem.html

- **GARFIELD** (Störung der Immunregulation)
  - **G** – Granulome
  - **A** – Autoimmunität
  - **RFI** – Rezidivierendes Fieber
  - **E** – Ekzematöse Hauterkrankungen
  - **L** – Lymphoproliferation
  - **D** – Darmentzündung

https://tmnt.fandom.com/de/wiki/Garfield

Was sind klinische Hilfsmittel?

- Z.B. Grimbacher Score, IUIS-Klassifikation, PID-App

Table 1

Scoring System with Clinical and Laboratory Tests for Individuals in Kindreds with HIES

	Points[a]									
Clinical Findings	0	1	2	3	4	5	6	7	8	10
Highest serum-IgE level (IU/ml)[b]	<200	200–500			501–1,000				1,001–2,000	>2,000
Skin abscesses	None		1–2		3–4				>4	
Pneumonia (episodes over lifetime)	None		1		2		3		>3	
Parenchymal lung anomalies	Absent						Bronchiectasis		Pneumatocele	
Retained primary teeth	None	1	2		3				>3	
Scoliosis, maximum curvature	<10°		10–14°		15°–20°				>20°	
Fractures with minor trauma	None				1-2				>2	
Highest eosinophil count (cells/μl)[c]	<700			700–800			>800			
Characteristic face	Absent		Mildly present			Present				
Midline anomaly[d]	Absent					Present				
Newborn rash	Absent				Present					
Eczema (worst stage)	Absent	Mild	Moderate		Severe					
Upper respiratory infections per year	1-2	3	4–6		>6					
Candidiasis	None	Oral	Fingernails		Systemic					
Other serious infections	None				Severe					
Fatal infection	Absent				Present					
Hyperextensibility	Absent				Present					
Lymphoma	Absent				Present					
Increased nasal width[e]	<1 SD	1–2 SD		>2 SD						
High palate	Absent		Present							
Young-age correction	>5 years			2–5 years		1–2 years		≤1 year		

[a] The entry in the furthest-right column is assigned the maximum points allowed for each finding.
[b] Normal <130 IU/ml.
[c] 700/μl = 1SD, 800/μl = 2 SD above the mean value for normal individuals.
[d] For example, cleft palate, cleft tongue, hemivertebrae, other vertebral anomaly, etc. (see Grimbacher et al. 1999*a*).
[e] Compared with age- and sex-matched controls (see Farkas et al. 1994).

Grimbacher et al. 1999; https://doi.org/10.1086/302547

Momentane Interpretation:
> 40 Pkt: HIES
20-40 Pkt: V.a. HIES
< 20 Pkt: kein HIES

Journal of Clinical Immunology (2020) 40:66–81
https://doi.org/10.1007/s10875-020-00758-x

ORIGINAL ARTICLE

Check for updates

Human Inborn Errors of Immunity: 2019 Update of the IUIS Phenotypical Classification

Aziz Bousfiha[1,2] · Leila Jeddane[3] · Capucine Picard[4,5] · Waleed Al-Herz[6] · Fatima Ailal[1] · Talal Chatila[7] · Charlotte Cunningham-Rundles[8] · Amos Etzioni[9] · Jose Luis Franco[10] · Steven M Holland[11] · Christoph Klein[12] · Tomohiro Morio[13] · Hans D. Ochs[14] · Eric Oksenhendler[15] · Jennifer Puck[16] · Troy R. Torgerson[14] · Jean-Laurent Casanova[17,18,19,20] · Kathleen E. Sullivan[21] · Stuart G. Tangye[22,23]

Received: 12 December 2019 / Accepted: 22 January 2020 / Published online: 11 February 2020

PID Classification

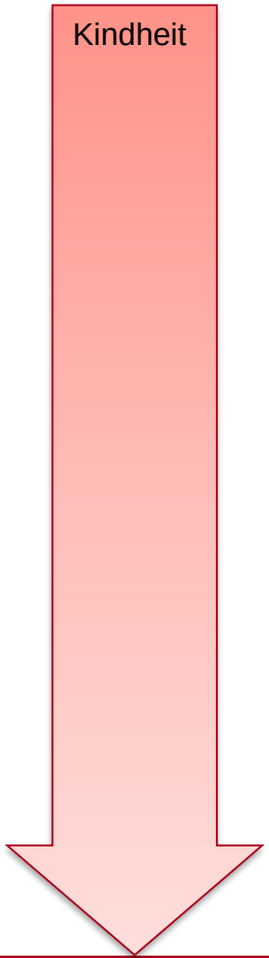
- Classification tables
- Search disease by name
- Search by manifestation
- How to explore PID
- Normal values

Fallbeispiele

Schwere Ekzeme im Rahmen von Immundefekten

1. Fall: Lena *1990

Anamnese



- rezidivierende Atemwegsinfekte
- 1994 Pneumonie → Teilresektion bei infizierter Lungenzyste
- 1996 Pneumonie
- 1997 Glutealabszess bei Z. n. Injektion
- gestörte Exfoliation der Milchzähne
- 1998 Unterarmfraktur bei Bagatelltrauma
- schweres atopisches Ekzem mit Superifektion der Exkoriationen
- Nagelmykosen

Liegt ein Immundefekt vor?

Ja

Vielleicht

Eher nicht

Nein

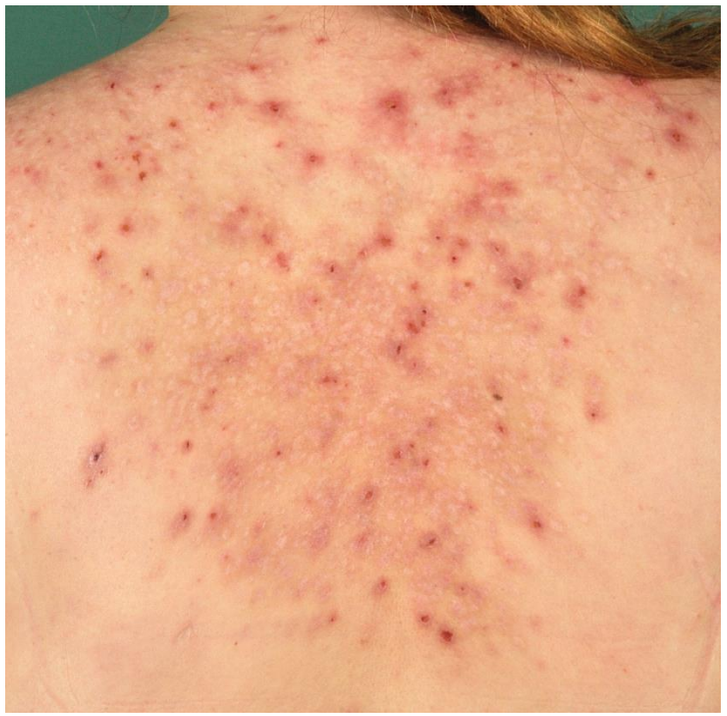
1. Fall: Lena *1990

Diagnose-stellung (ca. 12 Jahre)

→ **Beginn prophylaktische antibiotische Therapie**

→ **Beginn antimykotische Therapie**

→ **Beginn Immunglobulinsubstitution**

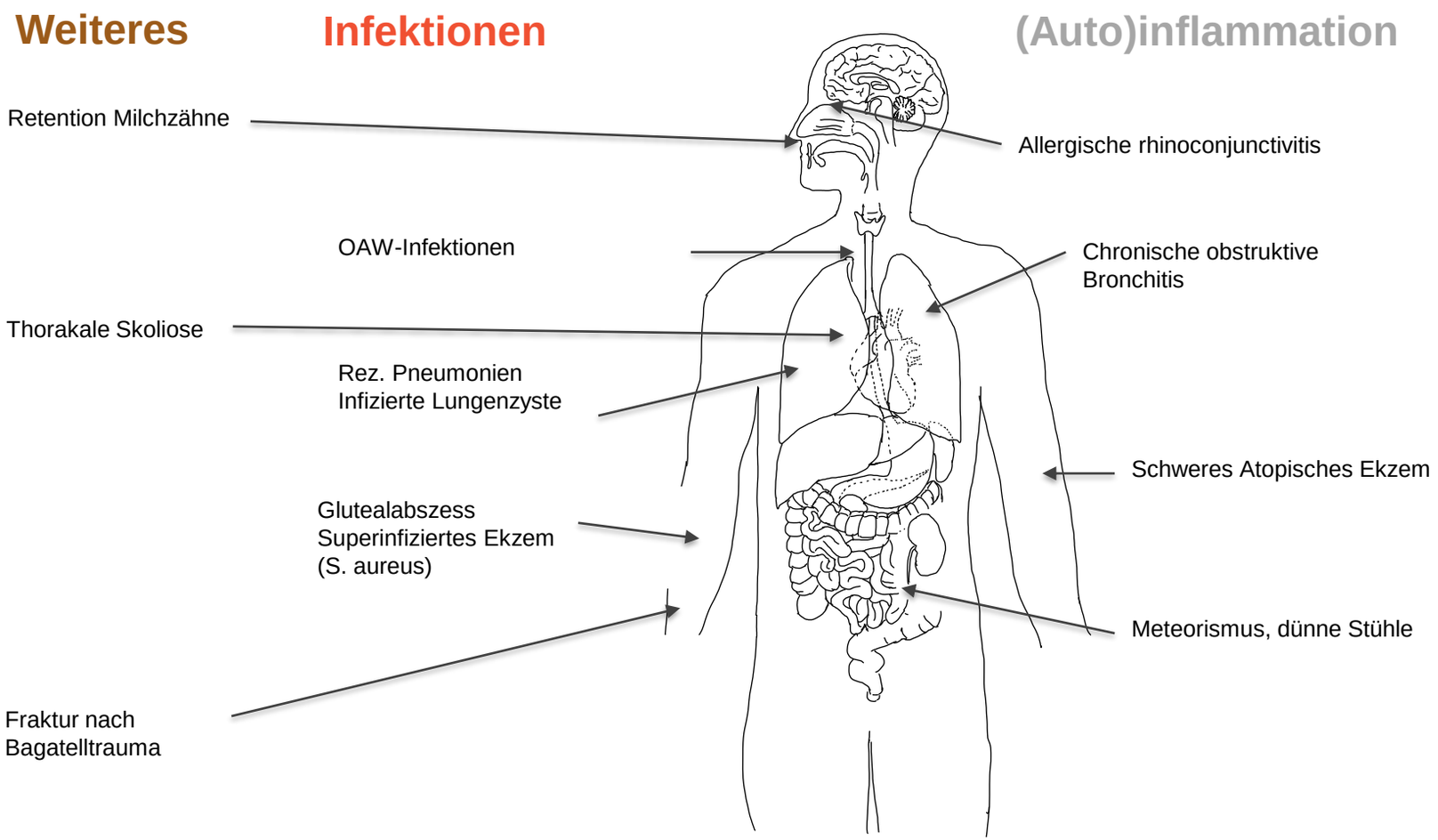


Erwach-senenalter

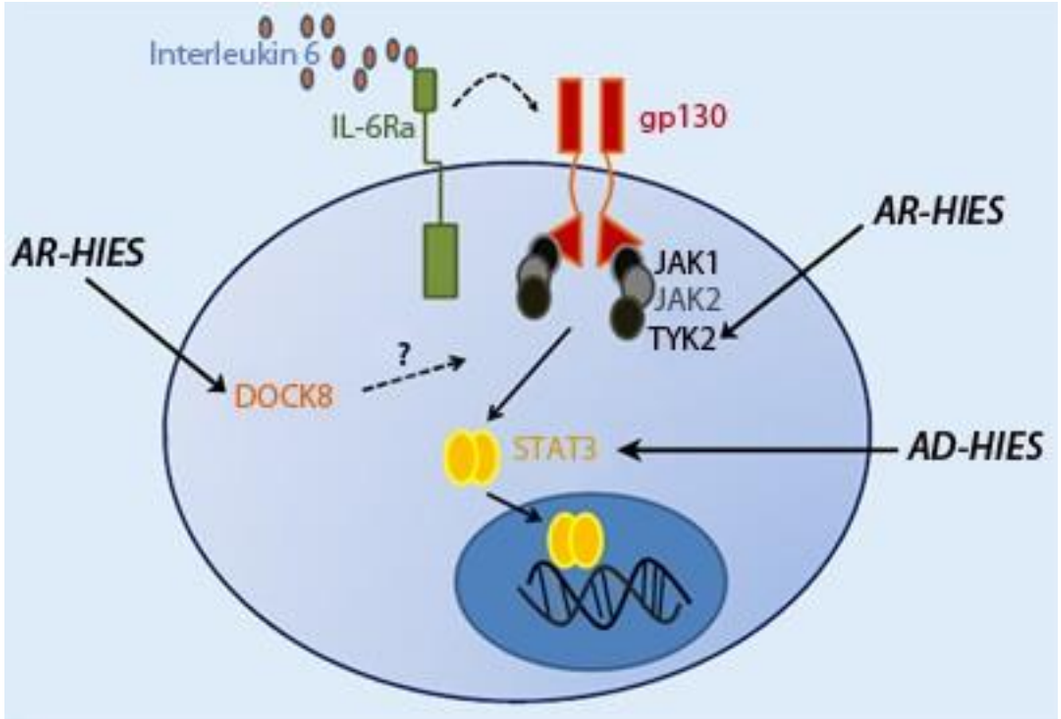
- atypische Pneumonie re. 09/2014
- atypische Pneumonie bds. 04/2018
- schweres atopisches Ekzem (Gesicht, Dekolletée, Rücken) mit Superifektion

→ **Besserung unter Dupilumab-Therapie**

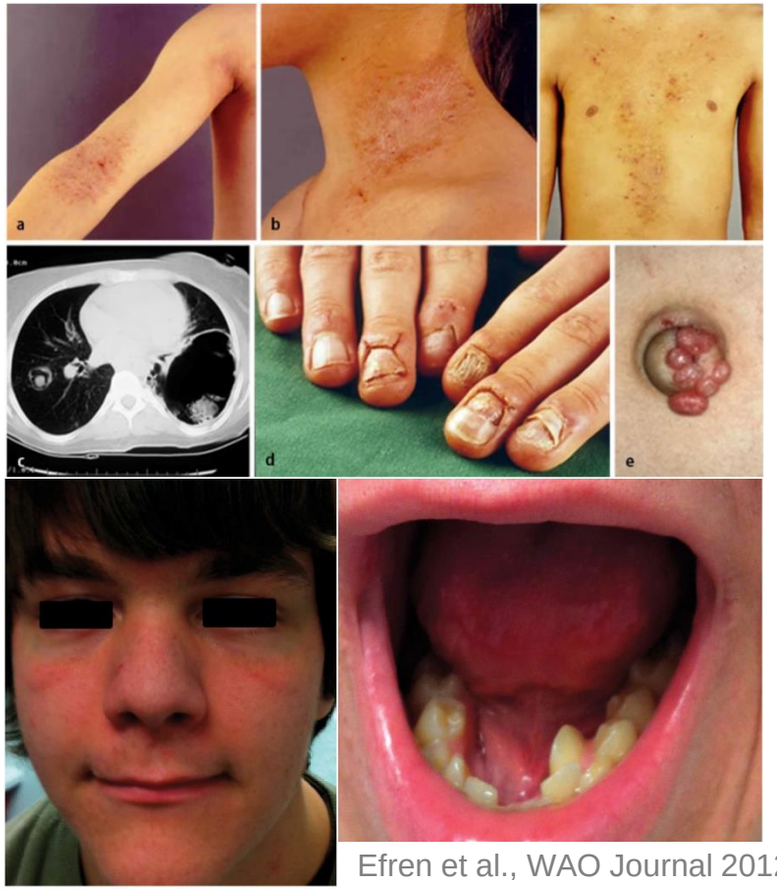
Klinischer Phänotyp



Klassisches Hyper-IgE-Syndrom (*STAT3*LOF)



Hagl et al., 2014



Hagl et al., 2014

Efren et al., WAO Journal 2012

2. Fall: Daniel *2002

Anamnese

2 Monate
- Mastoiditis
- Pneumonie
- Agranulozytose

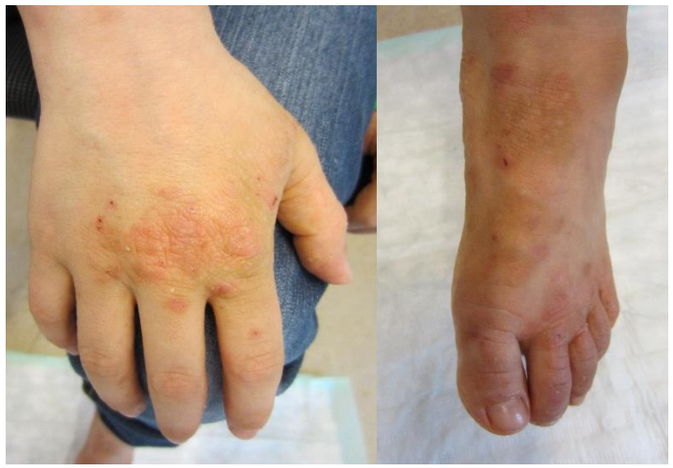
Kindheit
- Atopisches Ekzem
- Allergien
- Chronische Sinusitis
- Nagelmykosen

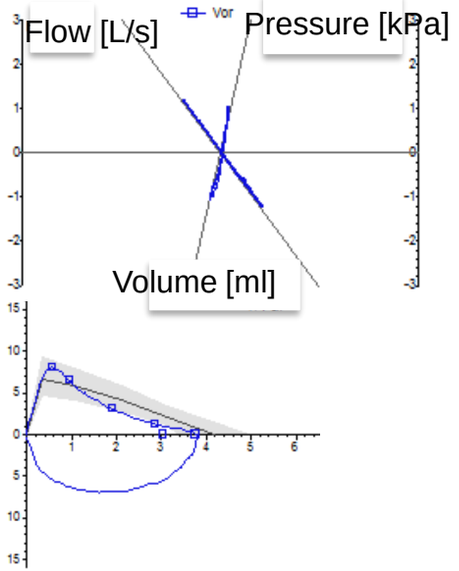
- Rez. Atemwegsinfekte

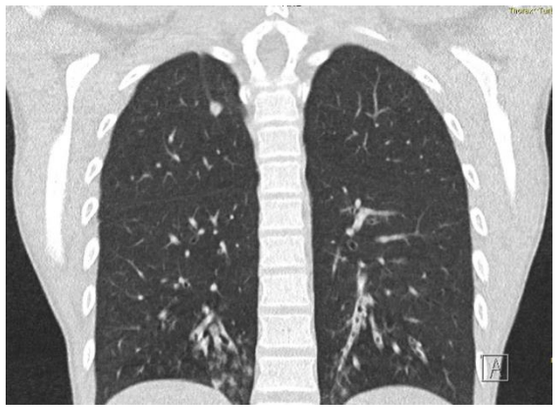
- Blutige Stühle

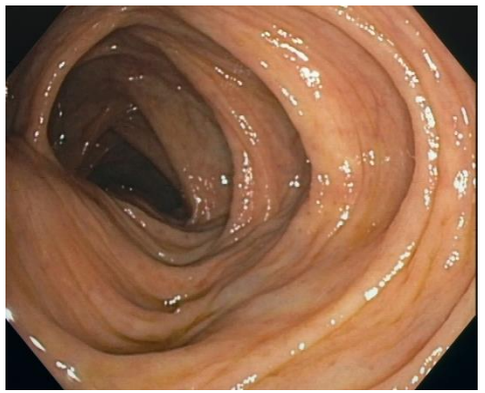
18 Jahre

Diagnostik









Gibt es „Red flags“?

Ja

Vielleicht

Eher nicht

Nein

Antwort: Gibt es “Red flags“?

Rez. Infektionen mit Hospitalisation

Agranulozytose

Bronchiektasen

Früher Beginn

Klinischer Phänotyp

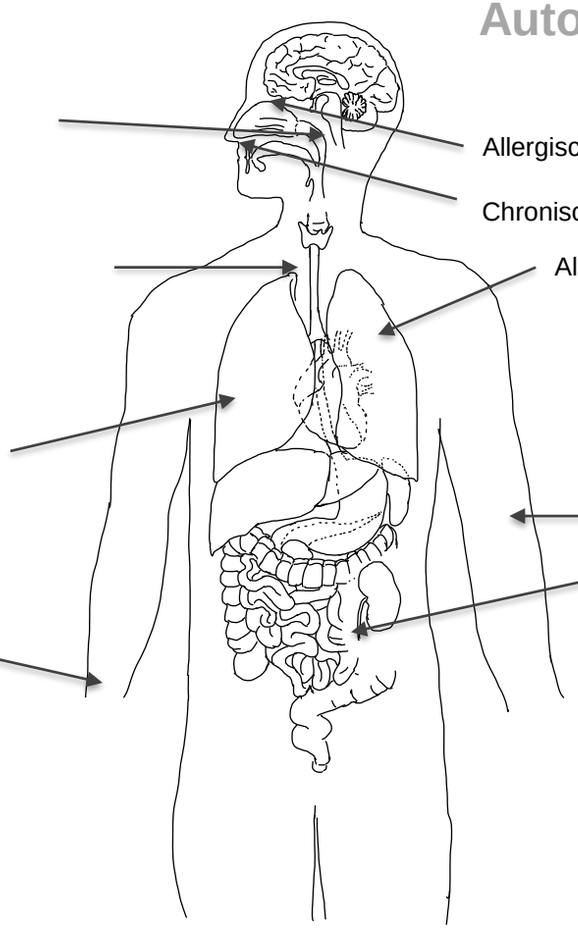
Infektionen

Mastoiditis

OAW-Infektionen

Pneumonie

Nagelmykosen



Autoinflammation

Allergische rhinoconjunctivitis

Chronische Sinusitis

Allergisches asthma(?)

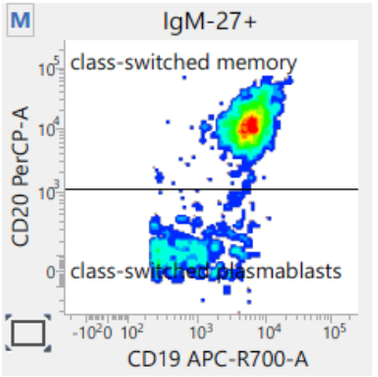
Atopisches Ekzem

Eosinophile Colitis

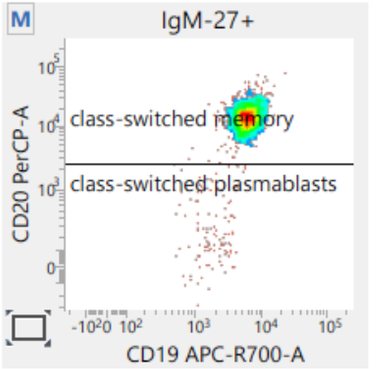
2. Fall: Daniel *2002

Diagnostik 2:
Labor + Immunphänotypisierung

- Eosinophilie (max. 5900/µL)
- Serum-IgE ↑(max. 1970kU/L)
- IgM and IgG ↓
- B-Zellen: klassengewechselte B-Zellen ↓
- T-Zellen: normale Anzahl und Subpopulationen
- T-Zell-Funktion: ↓Mitogene + spezifisch Antigene (tetanus)



Gesunde Kontrolle



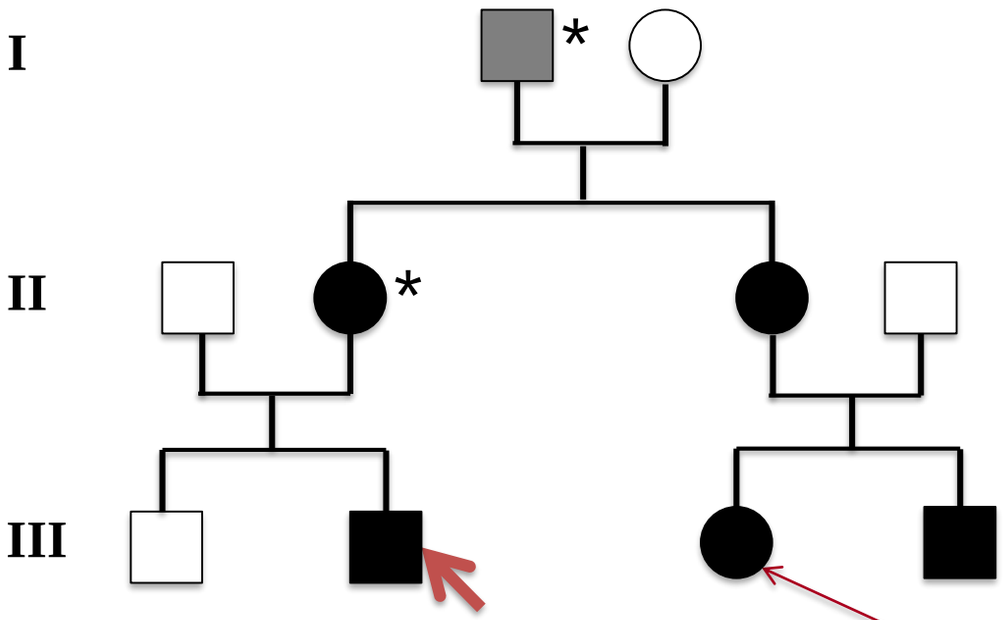
Patient

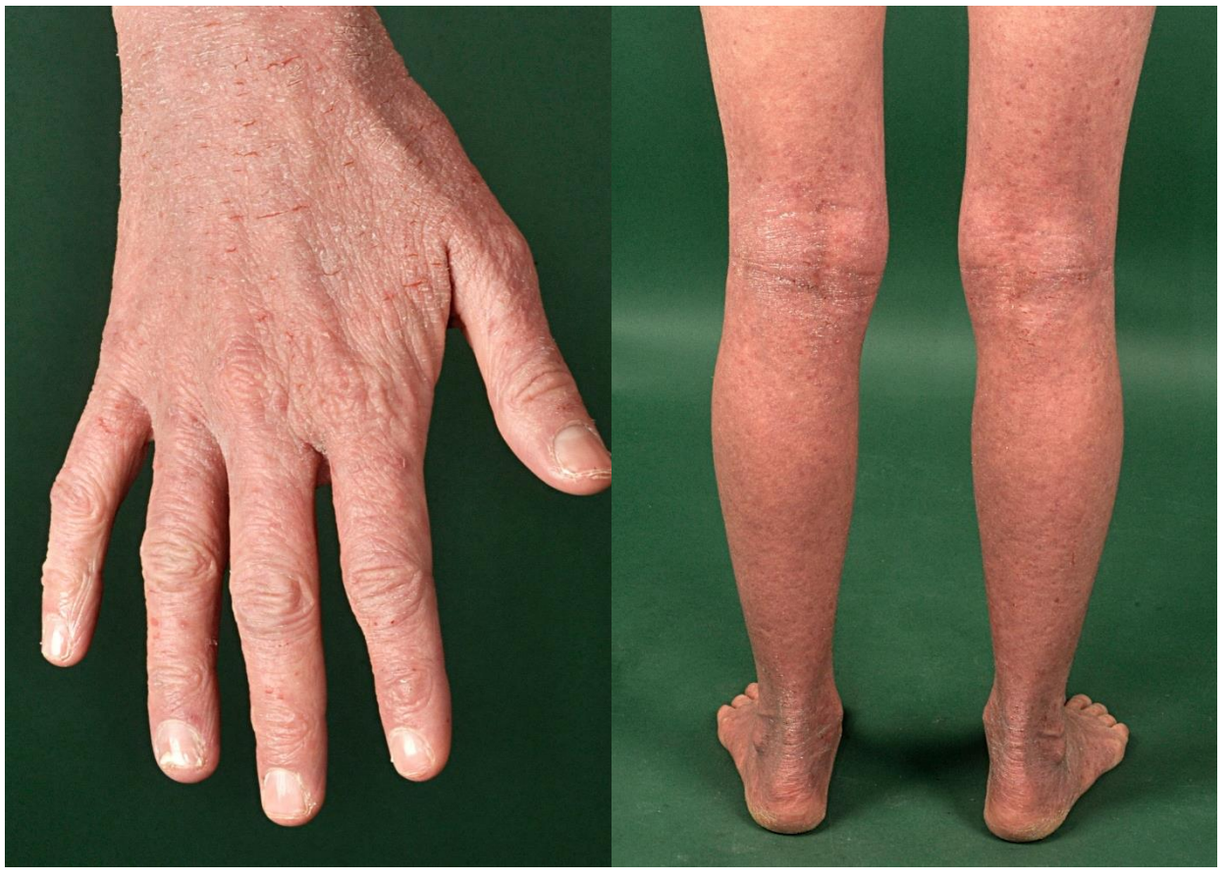
Genetische Untersuchung

- WES: heterozygote *CARD11* mutation p.(Arg75Trp)

2. Fall: Daniel *2002

Familienanamnese





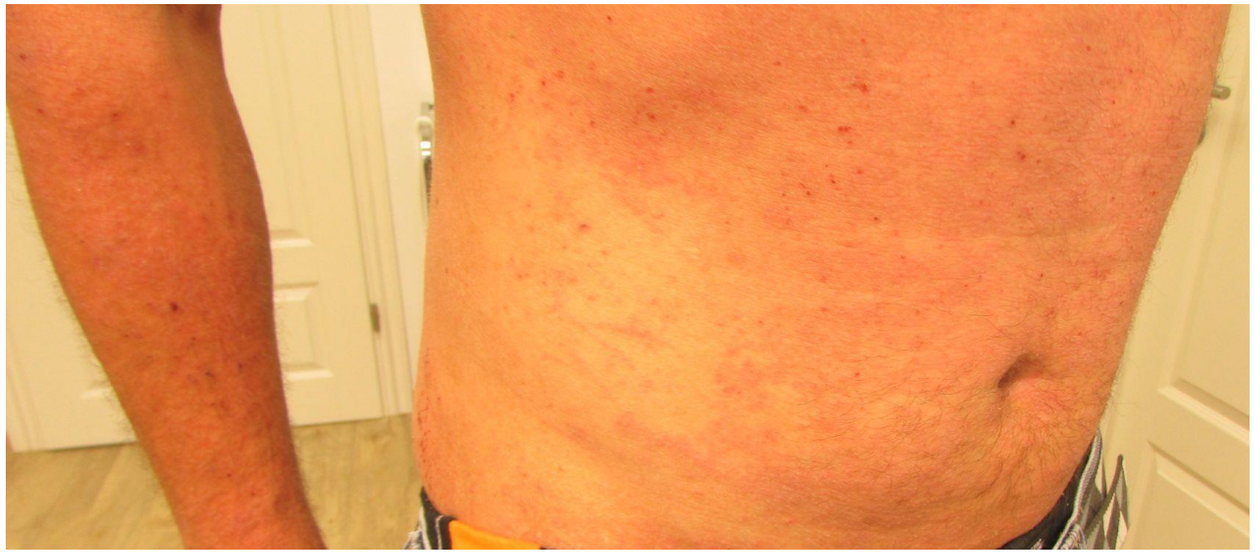
Legende:

- betroffen
- betroffen + genotypisiert: WT/p.(Arg75Trp)
- Nicht betroffen
- * Maligne Erkrankung
- Index-Patient

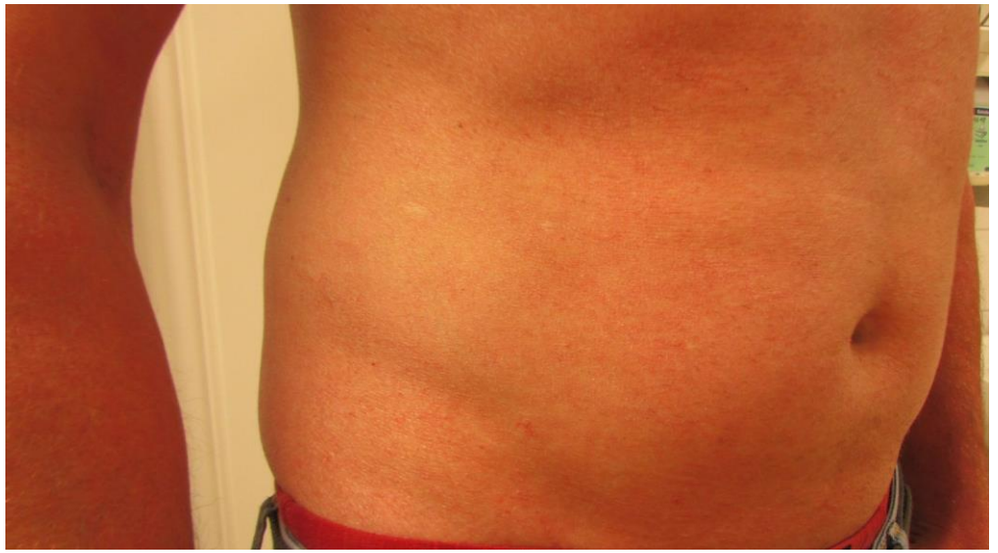
2. Fall: Daniel *2002

Dupilumab (IL4-, IL13-R AB)

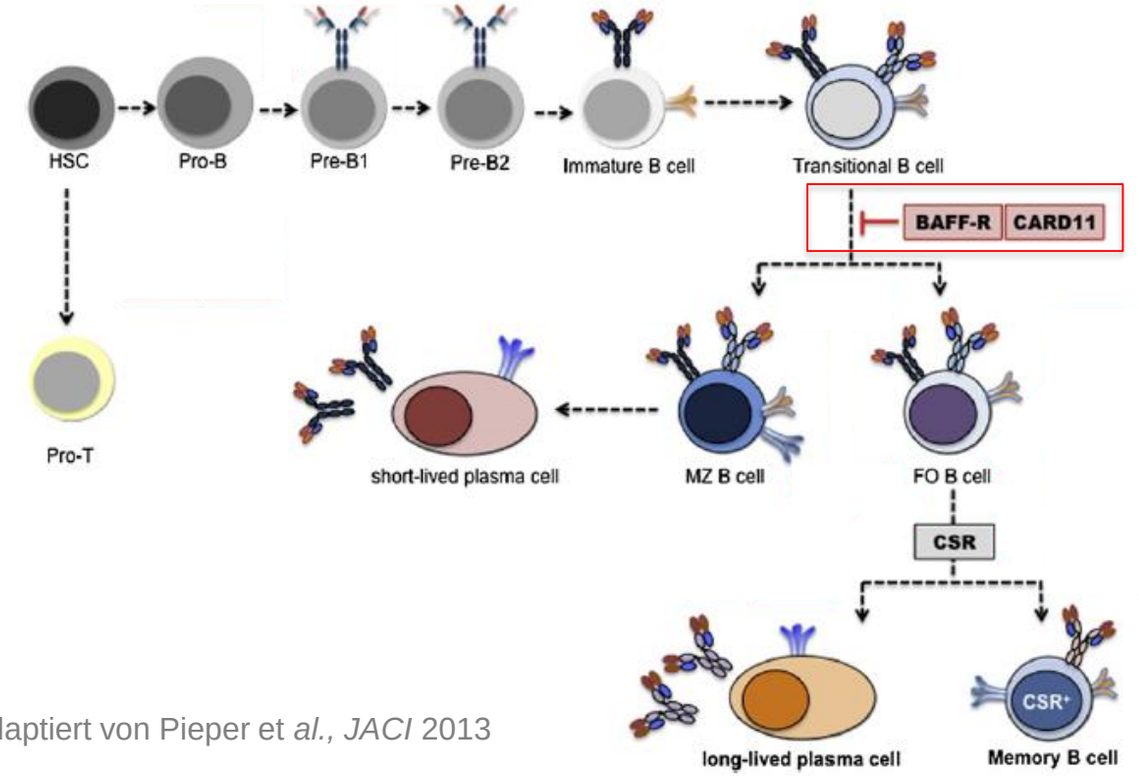
Vorher (SCORAD 67)



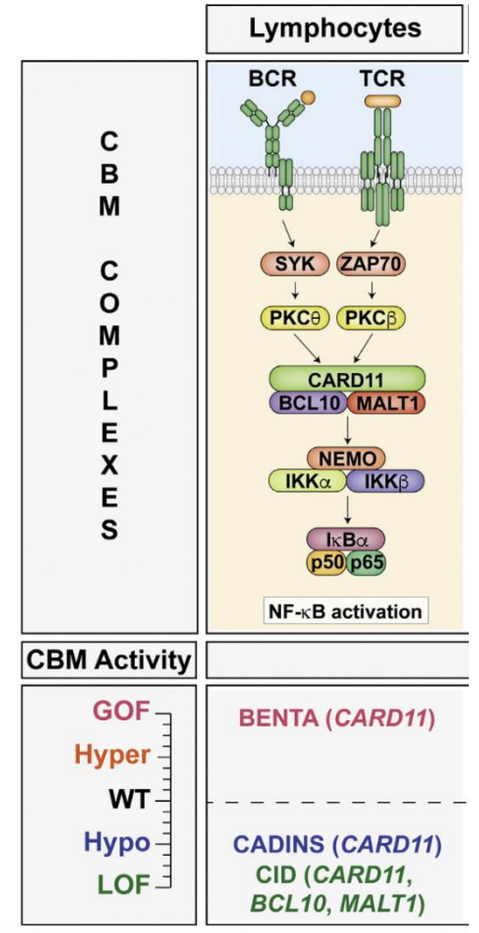
Nachher (SCORAD 17)



*CARD11*DN – CADINS disease



Adaptiert von Pieper et *al., JACI* 2013



Lu et al., 2019, *JACI*

3. Fall: Anna *2004

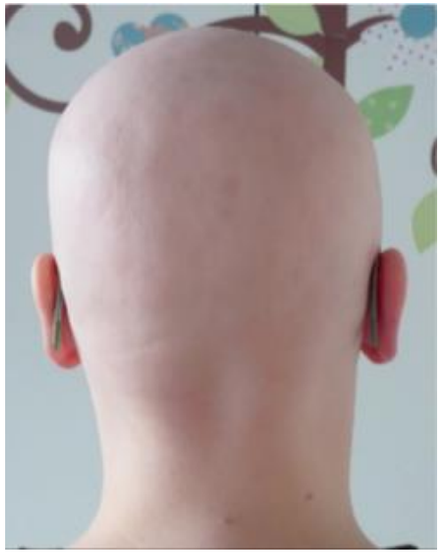
Anamnese

Kindheit

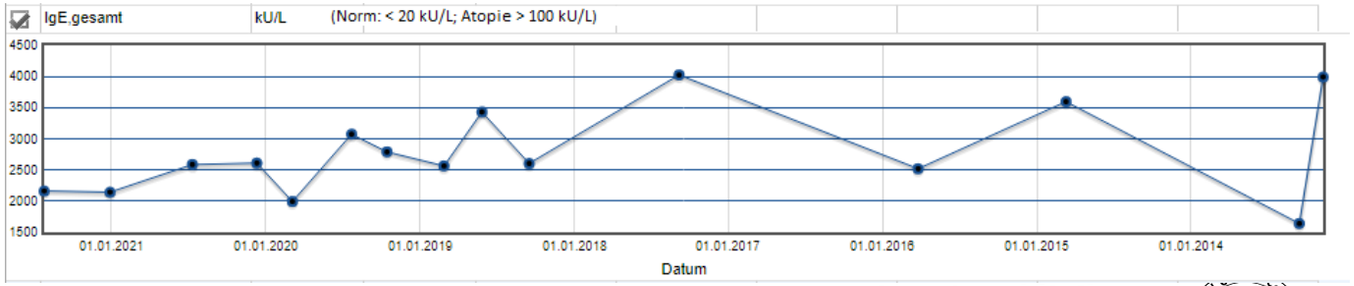
- Windeldermatitis, Ekzem als Säugling
- Asthma
- monatliche Atemwegsinfekte (Otitiden, Tonsillitiden, HWI)
- Persistierender Milchzahn

7 Jahre

- Alopezia totalis
- IgE ↑↑



IgE (Verlauf)



Liegt ein Immundefekt vor?

Ja

Vielleicht

Eher nicht

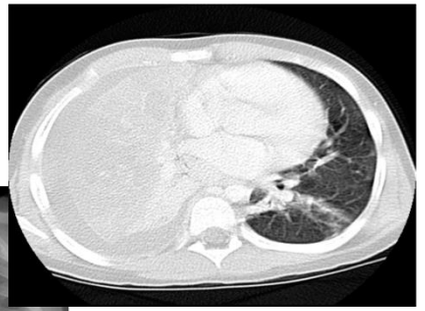
Nein

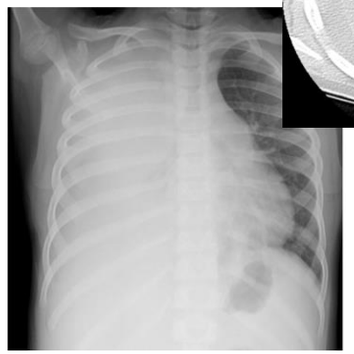
3. Fall: Anna *2004

Anamnese

9 Jahre

- Schwere Pneumonie mit Pleuraempyem
- Prologierte Beatmung, Sepsis





11 Jahre

- Chronische ITP

Blutbildveränderungen	Autoantikörper	Klinik
ITP (IVIG, Prednisolon, Eltrombopag, Romiplostim)	GP-Ia/IIa, GP-IIb/IIIa, GP-Ib/IX	Hämatome, Ekchymosen, Petechien
normozytäre, normochrome **Anämie**	Rhesus-Anti-Cw	Keine (insb. keine Hämolyse)

Kindheit/ Jugend

- Allergisches Asthma und Rhinokonjunktivitis
- Atopisches Ekzem

Klinischer Phänotyp

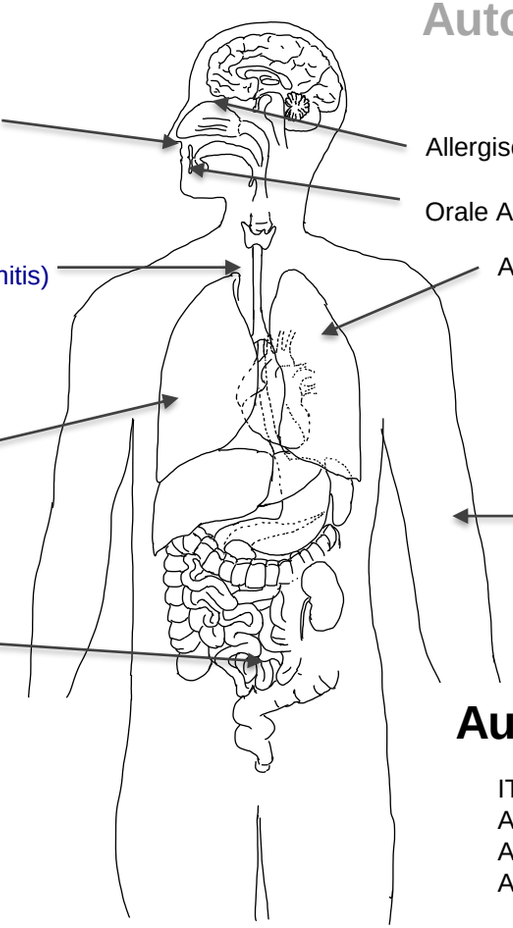
Infektionen

Dentogene Abszesse

OAW-Infektionen
(Otitis media, sinusitis, bronchitis)

Pneumonie (S. pneumoniae)
Empyem

HWI



Autoinflammation

Allergische rhinoconjunctivitis

Orale Aphthen

Allergisches asthma

Atopisches Ekzem
Rez. lokal HSV1
VZV-Reaktivierung

Autoimmunität

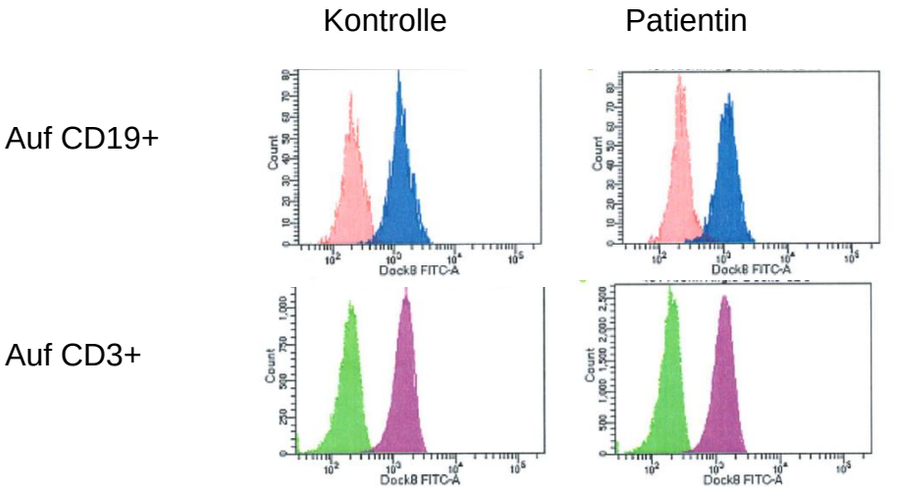
ITP
AI(H)A
AIN
Alopezie

3. Fall: Anna *2004

Diagnostik

Genetische Paneluntersuchung
(u.a. Heterozygote *DOCK8* Variante)

DOCK8-Expression

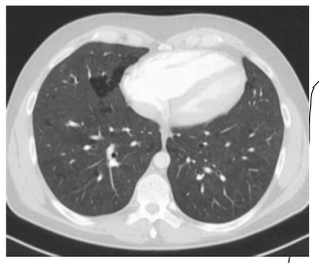


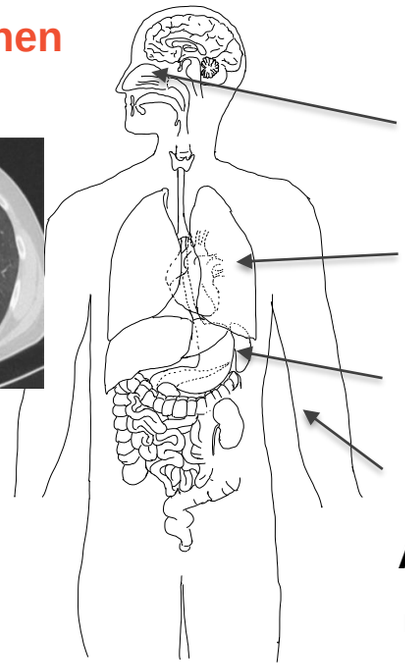
Immunologische Labordiagnostik

- **IgG, IgA, IgM normal**
- **T-Zellen**: Anzahl und Verteilung Subpopulationen ✓
- **T-Zell-Funktion**: Proliferation auf Mitogene ✓, spezifische Antigene (Tetanus) ↓
- **B-Zellen**: Anzahl und Verteilung Subpopulationen ✓

3. Fall: Anna *2004

Klinischer Phänotyp - Vater





Infektionen

Autoinflammation

Allergische rhinoconjunktivitis

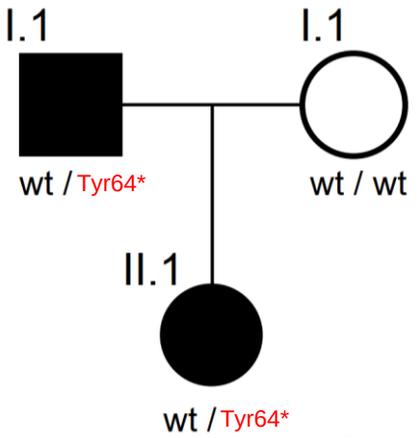
Organisierende pneumonie
Lymphadenopathie
Milchglastrübungen
Allergisches Asthma

Splenomegalie

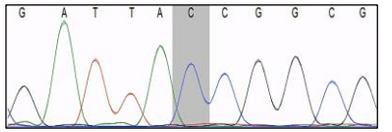
Atopisches Ekzem

Autoimmunität

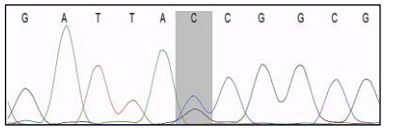
Hashimoto thyroiditis



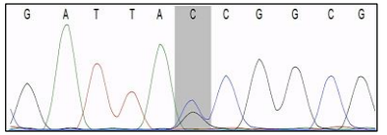
I.1



I.2



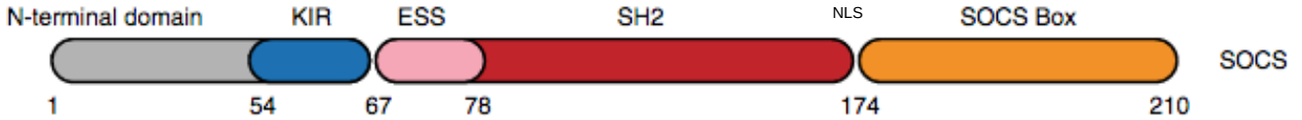
II.1



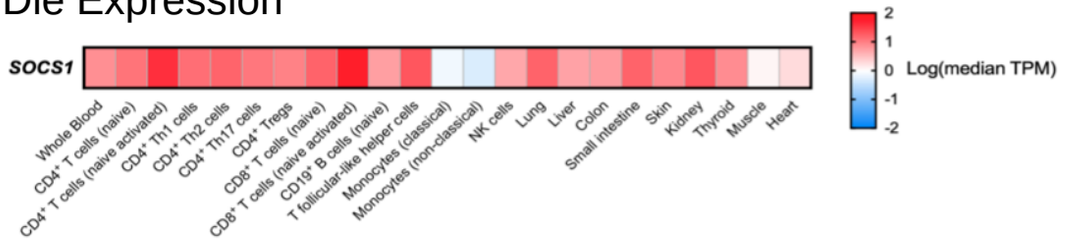
Whole exome sequencing (WES)

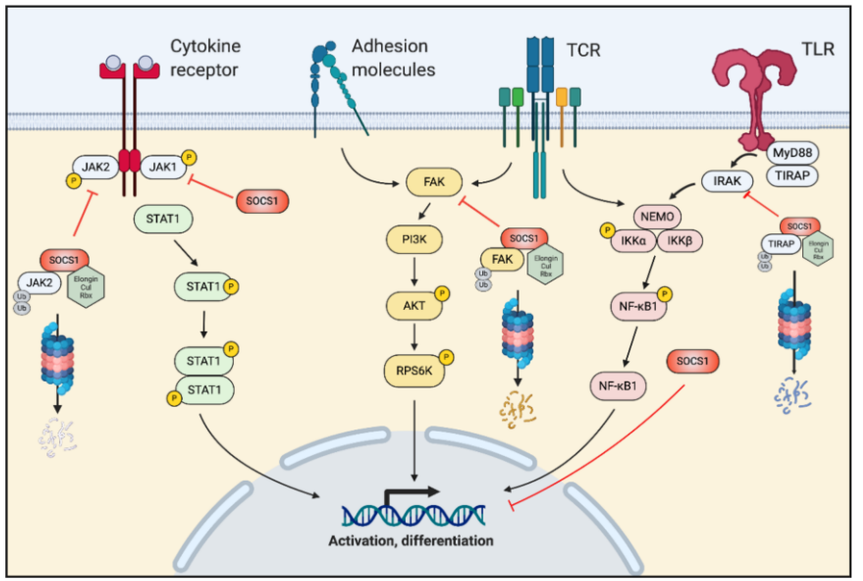
– Heterozygote *SOCS1*-Mutation (p.Tyr64*)

SOCS1 Haploinsuffizienz



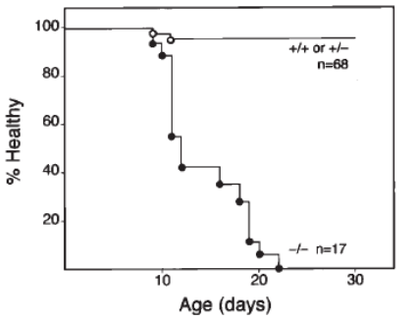
Die Expression





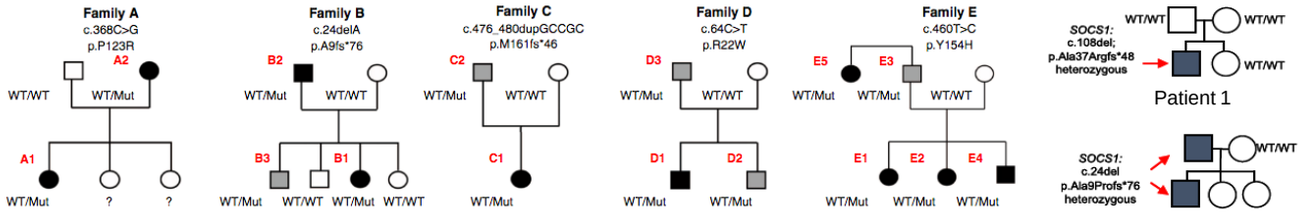
Körholz et al. 2021

Das Mausmodell (SOCS$^{-/-}$)



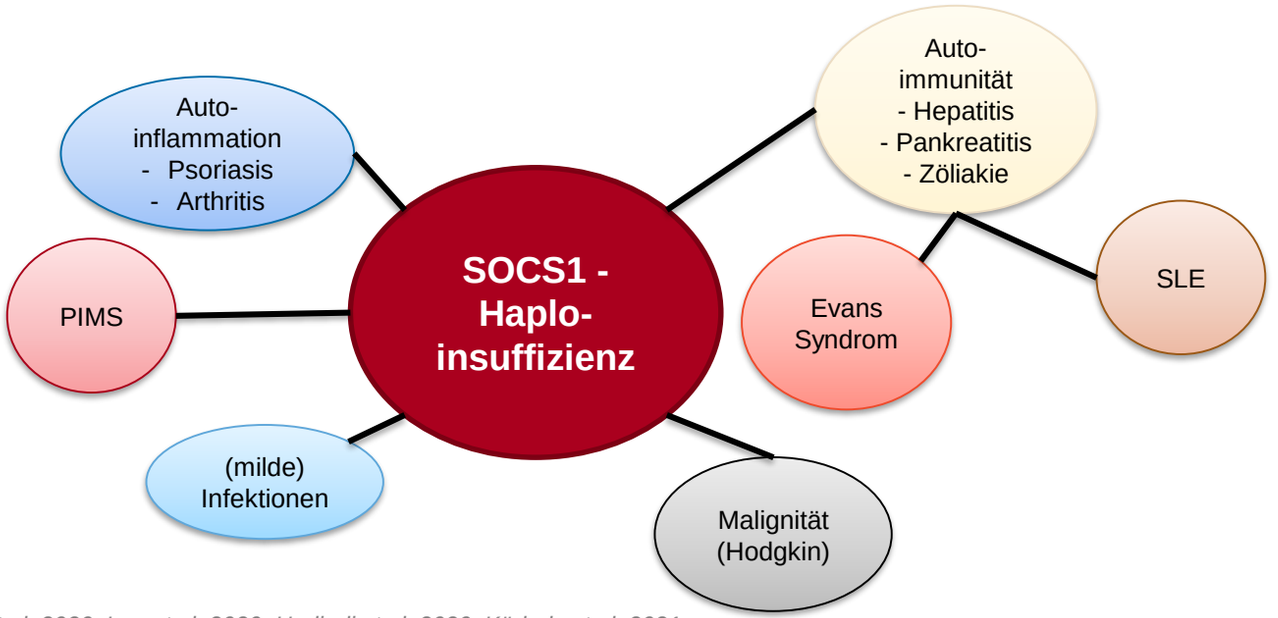
Starr et al. 1998

SOCS1 Haploinsuffizienz



Aus Hadjadj et al. 2020

Aus Lee et al. 2020



Vgl. Thaventhiran et al. 2020; Lee et al. 2020; Hadjadj et al. 2020, Körholz et al. 2021

4. Fall: Isabell *1989

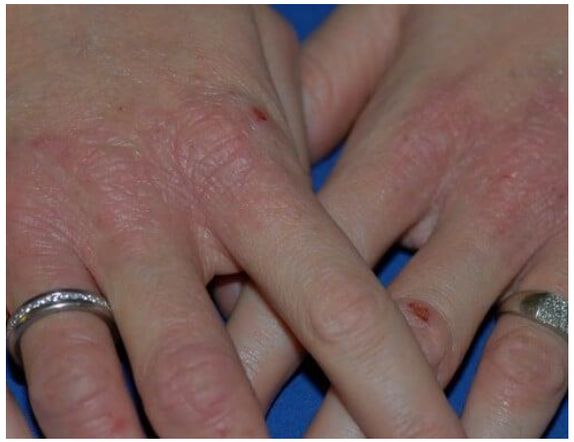
Anamnese

Kindheit

- Rez. Otitiden
- Rez. Sinusitiden
- Rez. Pneumonien (oft AB-Therapien, keine Hospitalisierung)

Seit der Jugend

- Atopie (Handekzem+ Allergische Rhinokonjunktivitis)



https://derma.plus/haut/handekzeme/

Liegt ein Immundefekt vor?

Ja

Vielleicht

Eher nicht

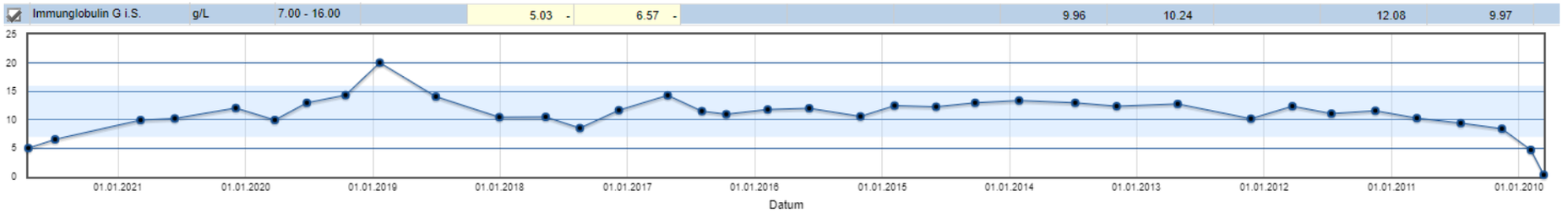
Nein

4. Fall: Isabell *1989

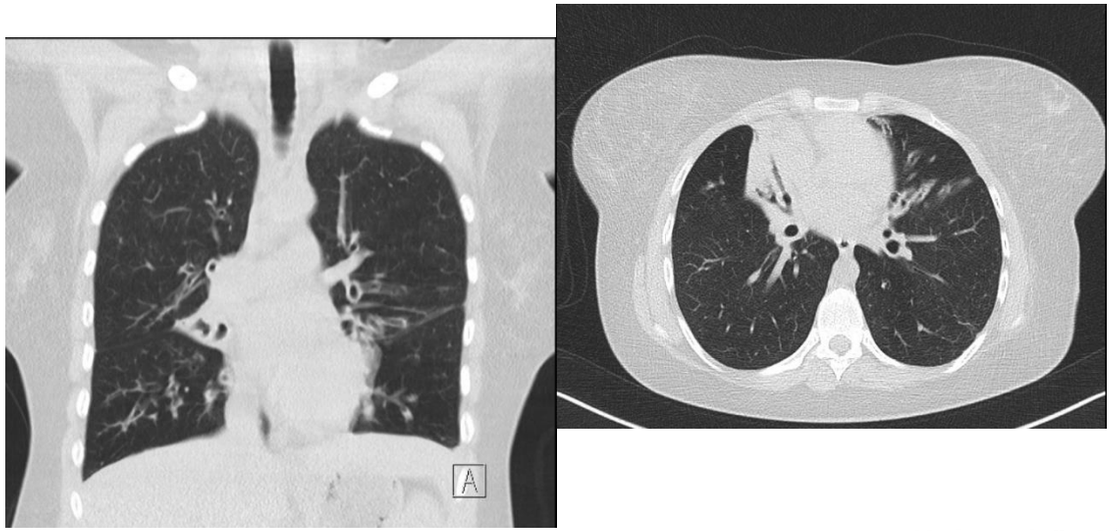
Beginn: IG-Substitution

Anamnese

16 Jahre
- Hypogammaglobulinämie
- Impftiter: fehlend



17 Jahre
- Bronchiektasen



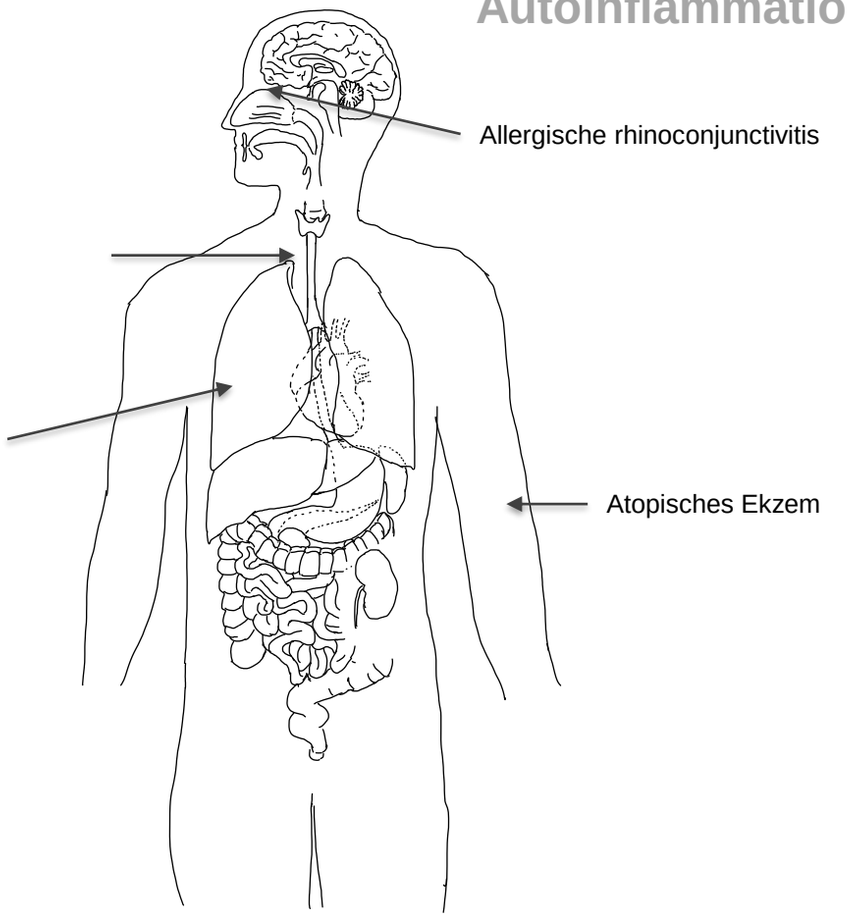
20 Jahre
- Schwere Pneumonie mit gekammertem Erguss

→ Operative Entlastung

Klinischer Phänotyp

Infektionen

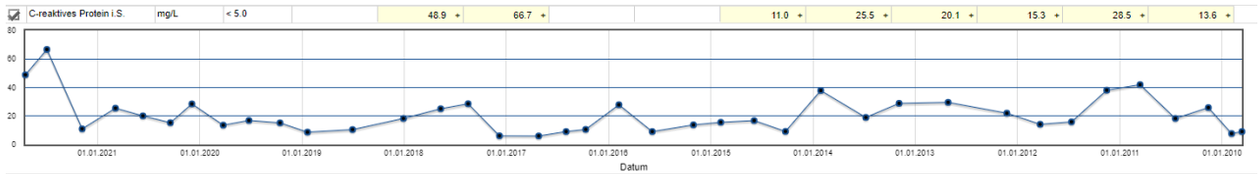
Autoinflammation



4. Fall: Isabell *1989

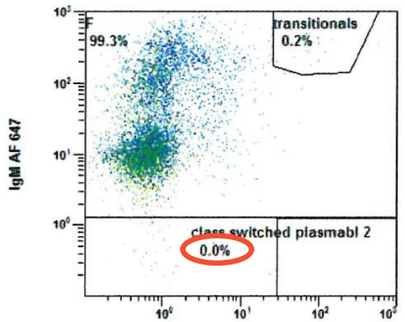
Laborergebnisse

- Keine Eosinophilie
- Serum-IgE normwertig
- Chronische Inflammation: CRP, BSG ↑

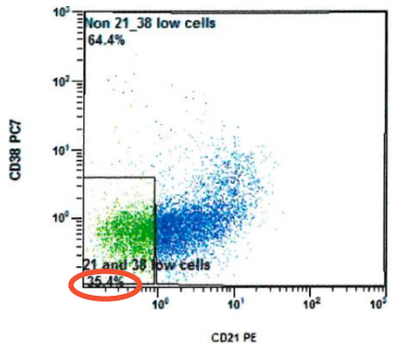


Immunphänotypisierung

- B-Zellen: milde B-Zell-Expansion (700/µL), B-Zell Klassenwechsel ↓, CD21low B-Zellen ↑
- T-Zellen: normale Anzahl, normale Verteilung der Subpopulationen



cs-Plasmablasten
Norm: 0,4 – 2,4 %



CD21low
Norm: 1,6 – 10 %

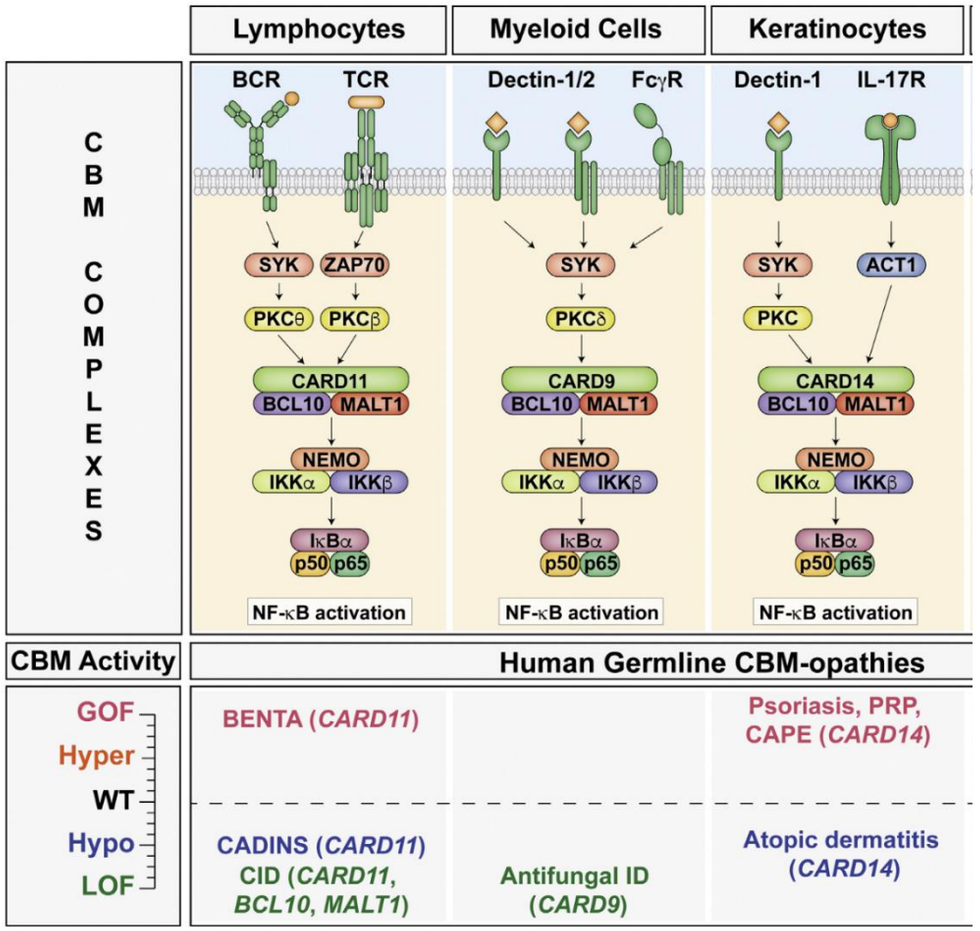
4. Fall: Isabell *1989

Genetische Untersuchung (WES)

- zunächst keine Treffer
- Nachbefundung: 2 VUS in ***CARD14*** (CC-Domäne)

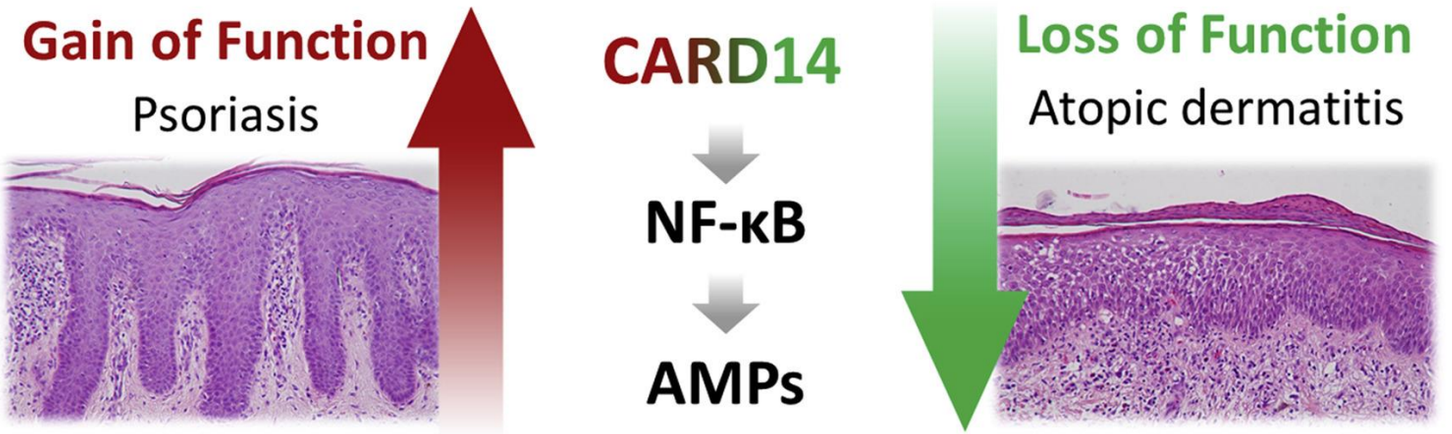
→ Funktionelle Validierung ausstehend

*CARD14*DN



Lu et al., 2019, *JACI*

Loss-of-function mutations in *CARD14* are associated with a severe variant of atopic dermatitis



NF-κB - nuclear factor kappa-light-chain-enhancer of activated B cells; AMPs - Antimicrobial peptides

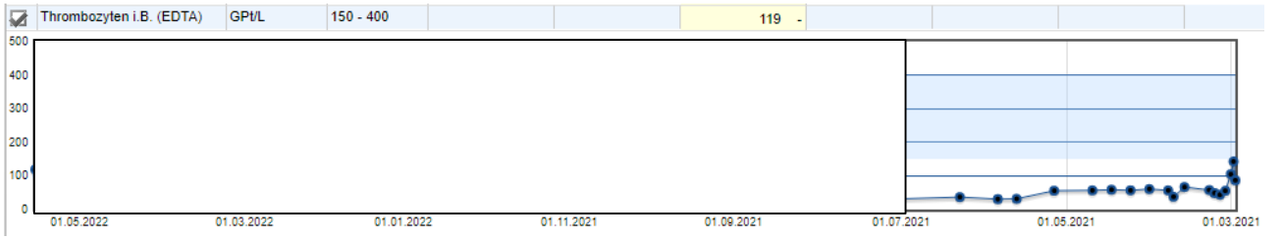
Peled et *al.*, *JACI* 2018

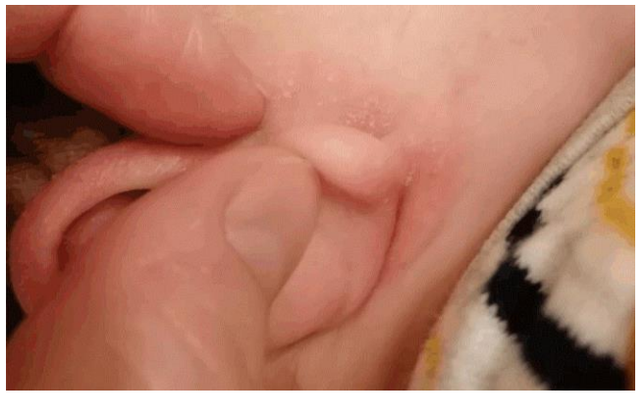
5. Fall: Leo *02.2021

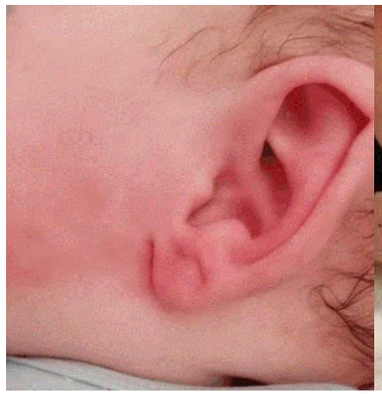
Anamnese

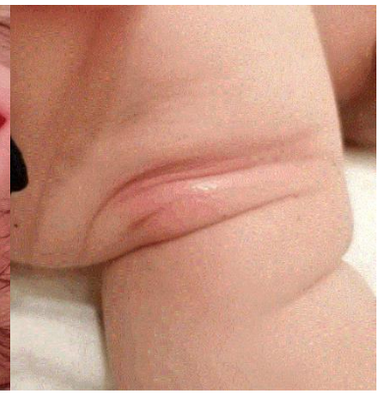
Säugling

- TREC-Screening unauffällig
- Milde Thrombozytopenie
- Mildes Ekzem









Gibt es „Red flags“?

Ja

Vielleicht

Eher nicht

Nein

Antwort: Gibt es “Red flags“?

Früher Beginn

Thrombozytopenie

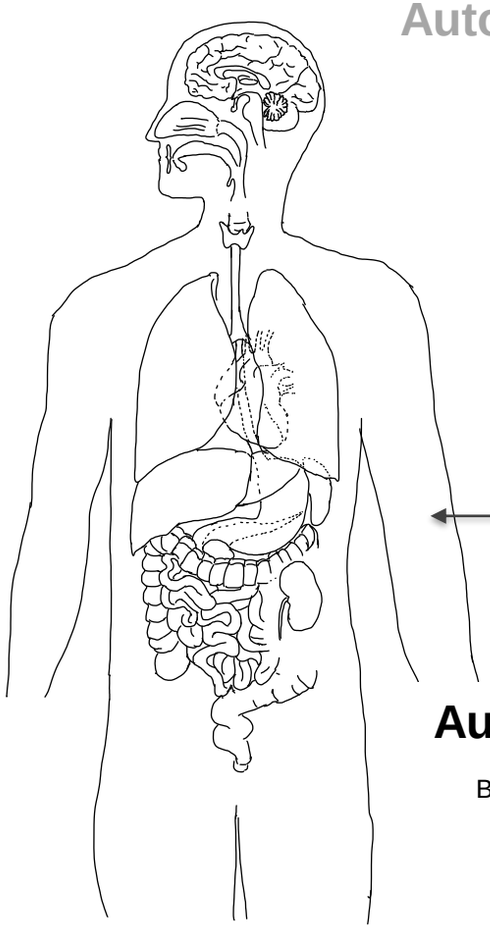
Klinischer Phänotyp

Weiteres

Thrombozytopenie

Infektionen

Bisher keine



Autoinflammation

Ekzem

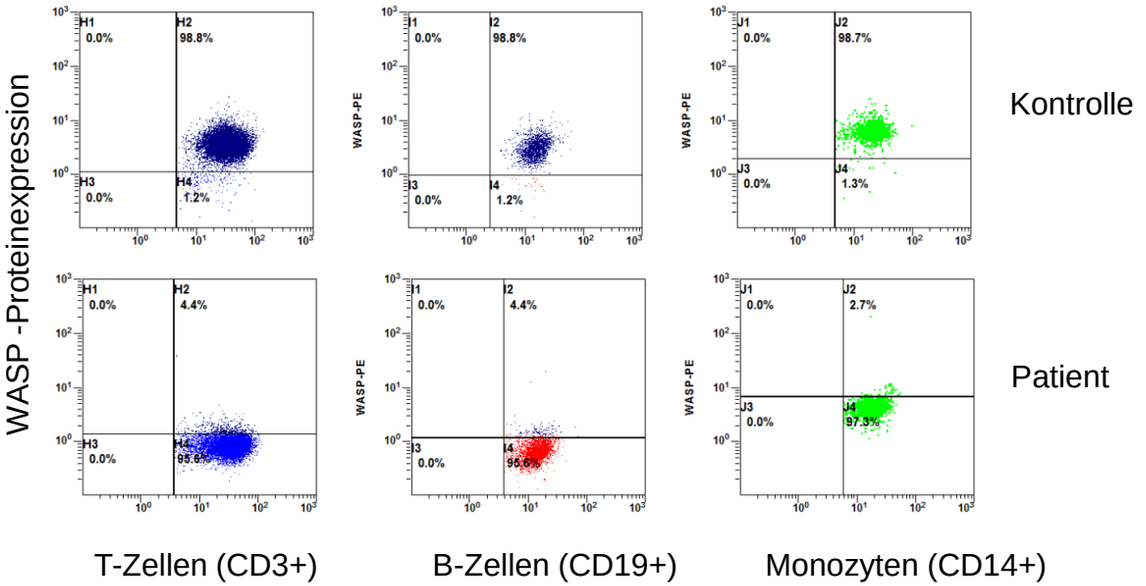
Autoimmunität

Bisher keine

5. Fall: Leo *02.2021

Laborergebnisse

- Imunglobuline: normwertig (IgA 0,07g/L, IgM 0,07g/L; IgG 4,38g/L)
- T-Zell-Immunphänotypisierung: weitgehend normal, CD8+ etwas verringert
- WASP-Proteinexpression: deutlich verringert



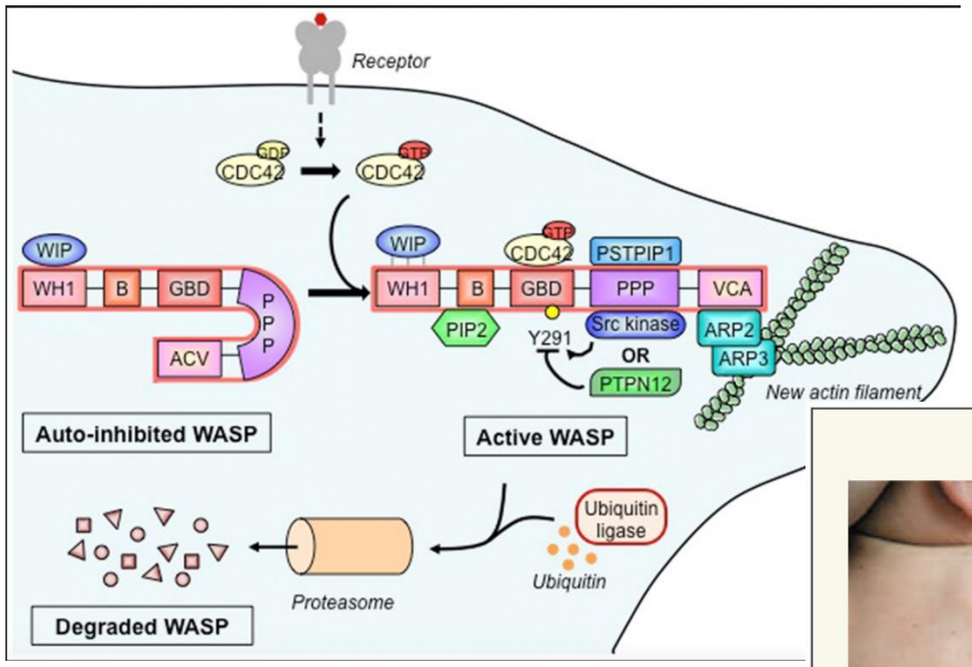
Genetische Untersuchung

- Insertion Exom 10 in *WAS*

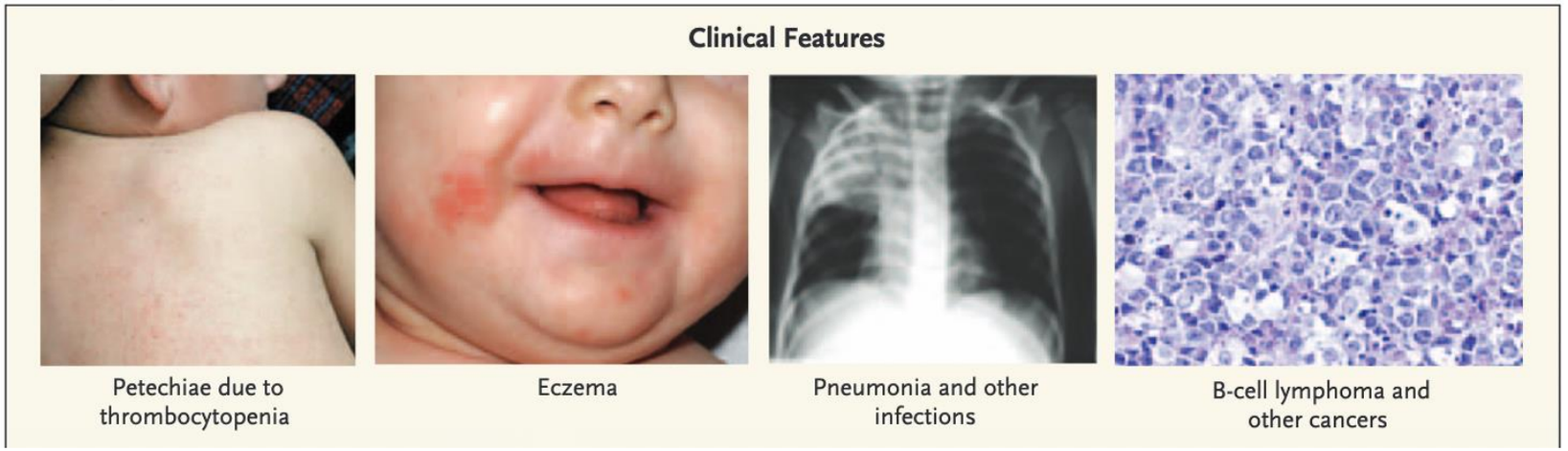
Therapie

- Allo HSCT von MUD 01/2022

WAS - Wiskott-Aldrich-Syndrom



Cotta-de-Almeida et *al.*, *FrontImmunology* 2015



Puck&Candotti, *NEJM* 2006

Zusammenfassung

Red Flags bei Kindern mit atopischem Ekzem beachten

- ELVIS, GARFIELD
- Familienanamnese

Klinische Praxis und therapeutische Ansätze

- Scores, IUIS-Klassifikation, Vorstellung Spezialambulanzen
- Biologicals, HSCT

Universitätsklinikum
Carl Gustav Carus
DIE DRESDNER.

Vielen Dank für Ihre Aufmerksamkeit.

Kontakt:
Julia Körholz
E-Mail: kik-anmeldung@ukdd.de

Adresse:
Universitätsklinikum Carl Gustav Carus
an der TU Dresden AöR
Klinik und Poliklinik für Kinder- und Jugendmedizin
Haus 21
Fetscherstraße 74, 01307 Dresden