Severe Combined Immunodeficiency

SCID T-B+NK+

An overview made by Ruben de Haan

What is T-B+NK+ SCID?

SCID is a group of auto-immune disorders caused by a mution in genes. T.B.NK. stands for the variant of SCID. For T-B+NK+ this means the patient lacks T-cells but has B-cells and NK-cells.

Basically the patients have no inner protection against bacteria and viruses.

A popular case was the ‘Boy In The Bubble’..

David Vetter aka the ‘Boy in the bubble’,

David lived for 12 years in a sterile bubble to protect him from infections and diseases.

Source: Wiki (wiki/David_Vetter)

Diagnosis:

In the first weeks after birth normally few problems occur, since the protectorcells of the mother are still present in the patient's blood.

±3 months

Then the patient's immune system begins to decline shown by red rash and vulnerablility to infections that do not heal.

You need white bloodcells to protect you.

- White bloodcells = leukocytes
- There are three main kinds:

Type:	T-cells	B-cells	NK-cells
Main function:	Help and kill other cells.	Produce antibodies.	Kill viruses and bacteria.

Problem:

The differences within SCID vary in what is lacking in the patient's blood in terms of leukocytes.

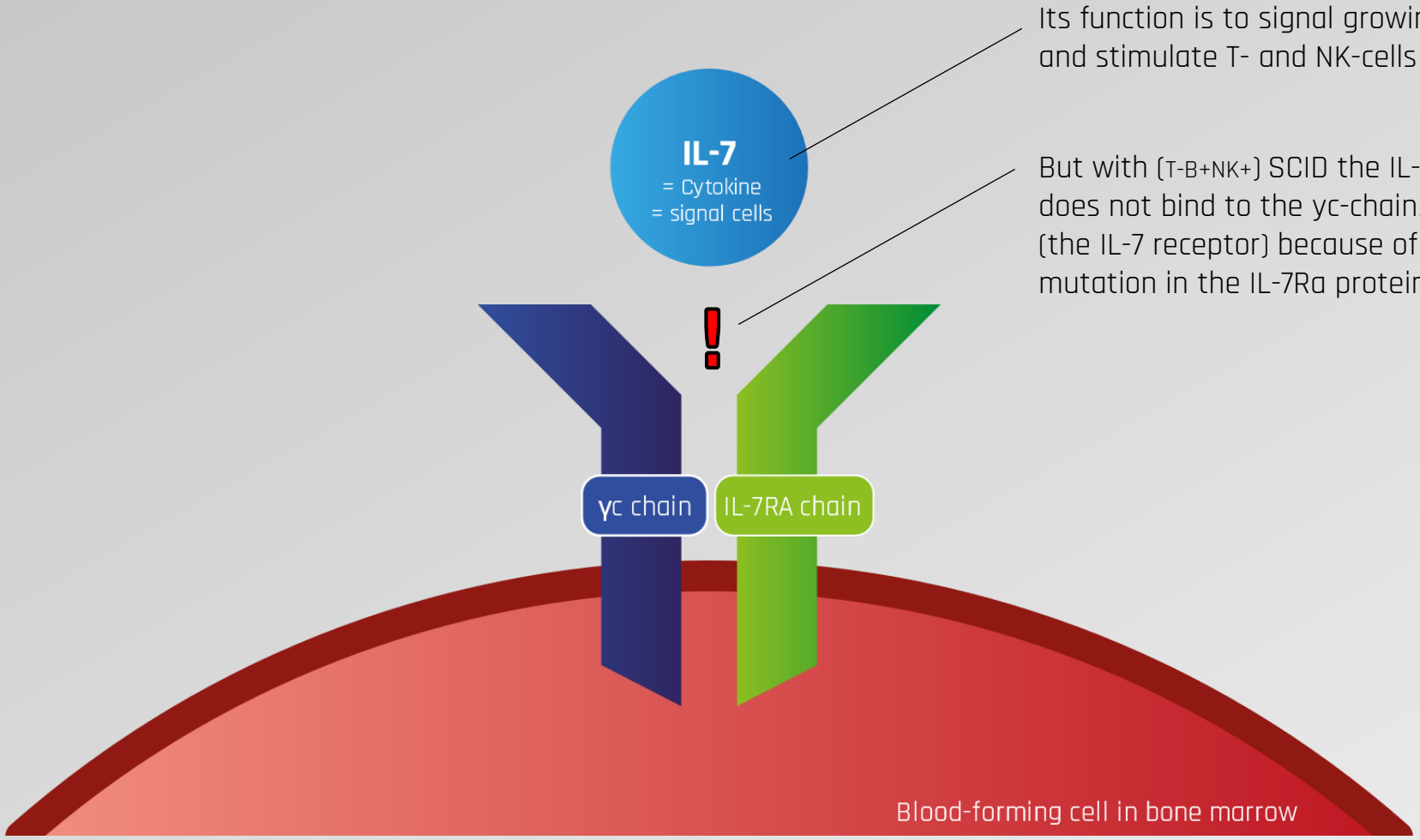
The different types of SCID:

Phenotype	±% of total SCID cases:	Gene Defect:	Pathogenic mechanism:
T-B+NK-	40%	JAK 3, Y-chain	Weakened cytokine signaling
T-B+NK+	10%	IL-7Ra	Weakened cytokine signaling
...	...	...	...

In the case of T-B+NK+ the following occurs:

Source: 'SCID: New and Old Scenarios', Informa Healthcare (www.informa-healthcare.com, 2012)

Problem on cellular level:



No IL-7 signalling means
no B-cell development & a lowered T-cell and NK-cell development and this means
no working immune system.

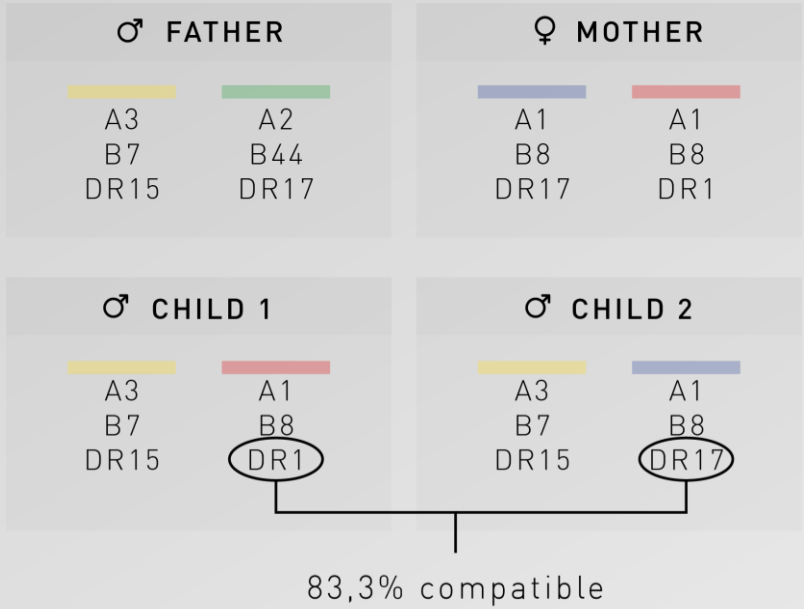
A current treatment:

1. Excluding HIV

2. Determining Lymphocytopenia
Checking blood to see that there are too few white blood cells.

3. Chemotherapy
Preparing the patient's blood for a bone marrow transplantation.

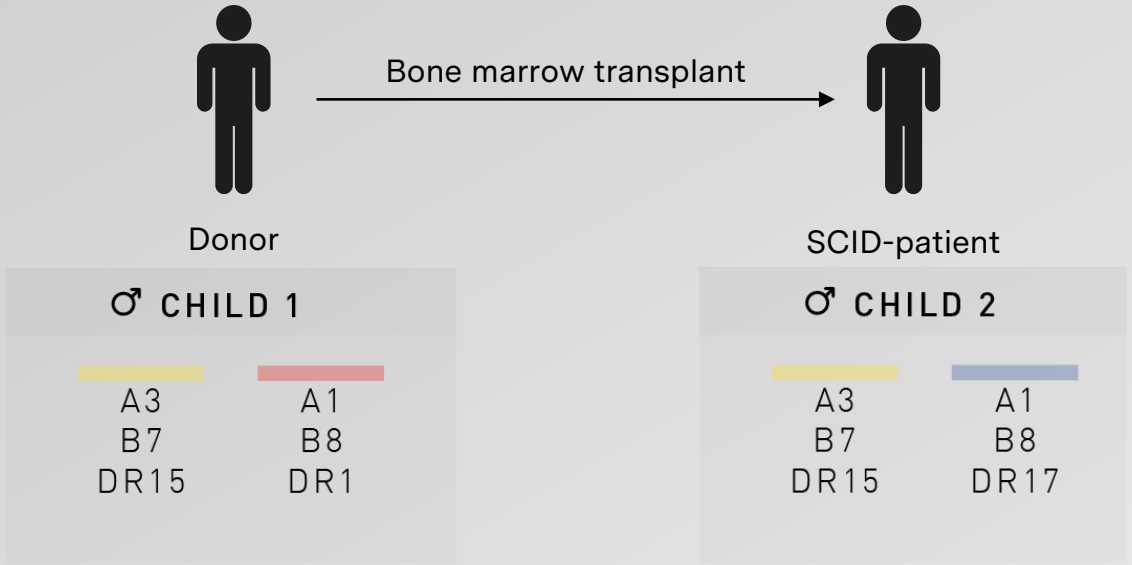
4. HLA screening:
HLA stands for *Human Leukocyte Antigen*. In a HLA screening the genes on the 6th chromosome are being determined to check for possible donor-compatibility. Example:



A current treatment:

5. Bone Marrow transplant

The bone marrow from the donor is (anesthetized) removed from the hipbone and infused in a vein of the patient, from where it flows to its bone cavities where it starts producing healthy leukocytes.



In

Conceptual proposal

Proposal:

		Deficient gene:
Cytokine Receptors	sub-unit:	IL2RG
	heterodimer:	IL2 IL4 IL7 IL9 IL15 IL21
	monomer:	IL7Ra

Using iGerm.org library to find a substitute protein for the IL7Ra monomer that realises a correct connection with the IL7 cytokine so that a working cell signalling is initiated.

Source: ESID patient register (www.esid.org, 2010)

References:

[1.] “Prevention of SUDEP” – P. Ryvlin, L. Nashef and T. Tomson.
[2.] “SCID; New and Old Scenarios” – G. Aloj, G. Giardino, L. Valentino, F. Maio, V. Gallo, T. Esposito, R. Naddei, E. Cirillo and C. Pignata.
[3] “'The Expanding Clinical and Immunological Spectrum of SCID' – M. van der Burg, A. R. Gennery.
[4] “IL7Rα Expression and Alternative Splicing” – C. Lundtoft, J. Seyfarth and M. Jacobsen.

Source: ESID patient register (www.esid.org, 2010)

End of overview