# 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 mutation in genes. T.B.NK. stands for the variant of SCID. For T-B+NK+ this means the patient lacks T-cells but does have active B-cells and NK-cells.

Basically the patients have no inner protection against bacteria and viruses. Which is life-threatening.

A popular case is the story of 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 expressed 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:

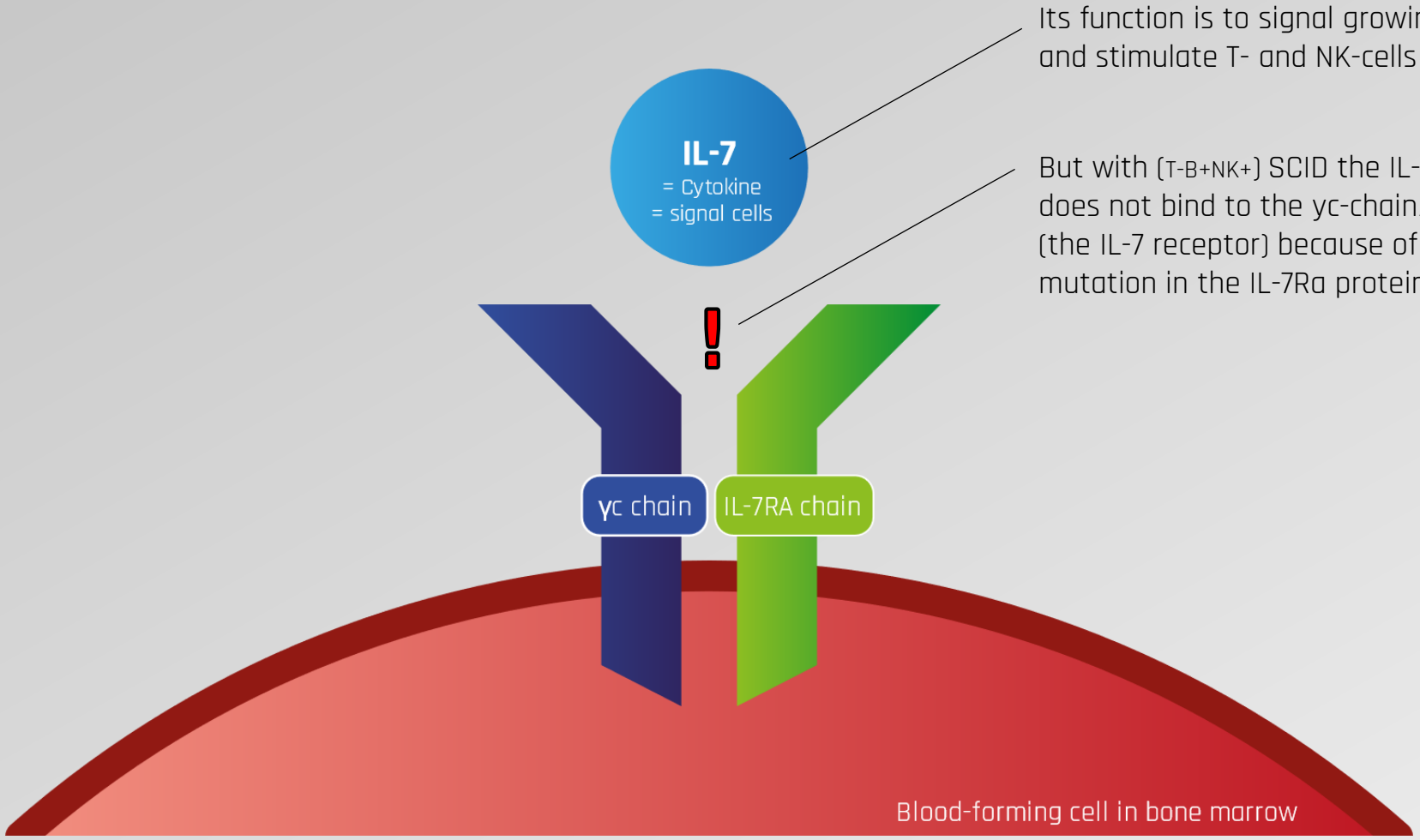
| Phenotype | ±% of total SCID cases: | Gene Defect: | Pathogenic mechanism: |
|---|---|---|---|
| T-B+NK- | 40% | JAK 3, Y-chain | Weakened cytokine signaling |
| T-B+NK+ | 10% | IL-7Ra | Weakened cytokine signaling |
| ... | ... | ... | ... |

## Result:

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.**

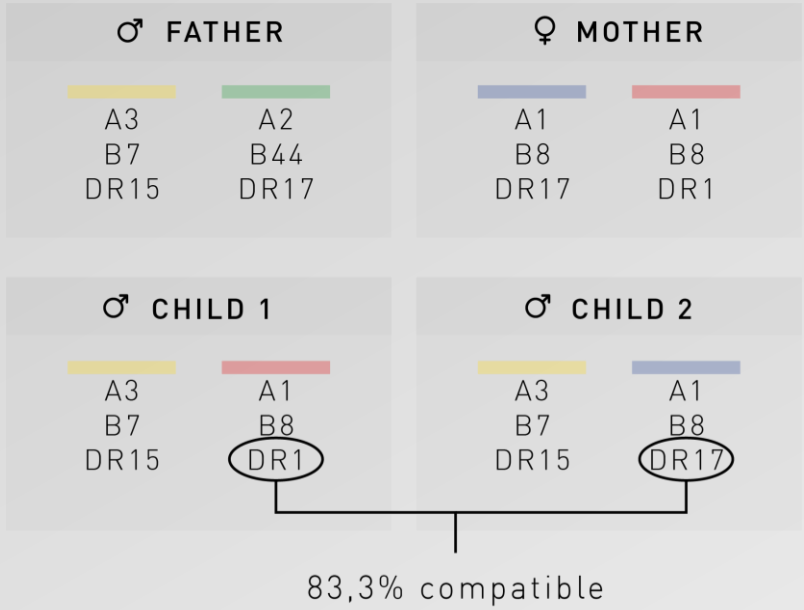
## A current treatment:

**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.

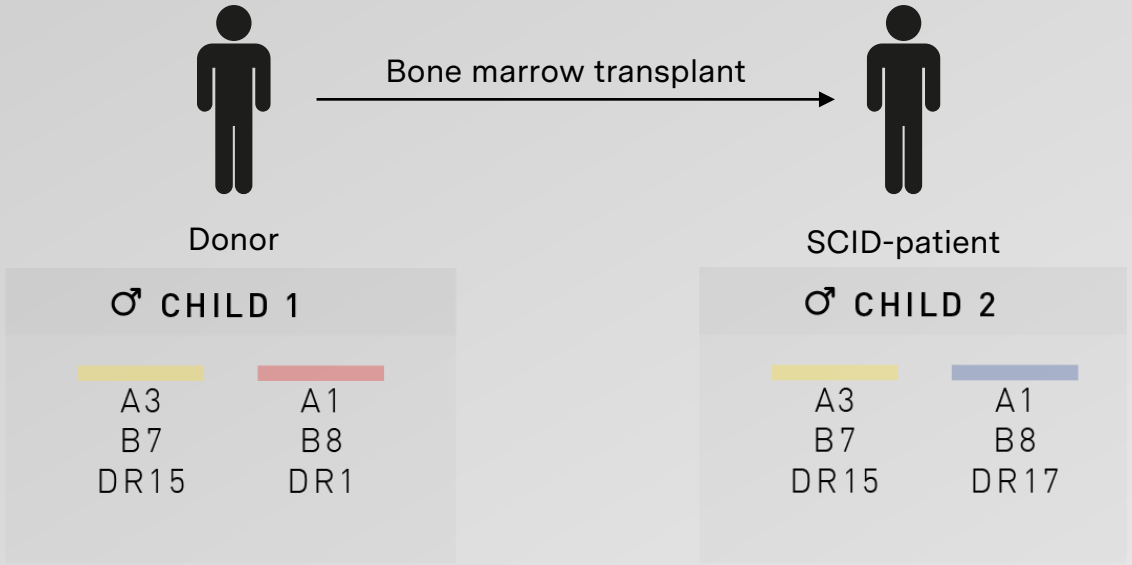
**4. HLA screening:**
HLA stands for *Human Leukocyte Antigen*. In a HLA screening the genes on the 6th chromosome are being determined to check for possible donor-compatibility. Example:



## 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.

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# Conceptual proposal

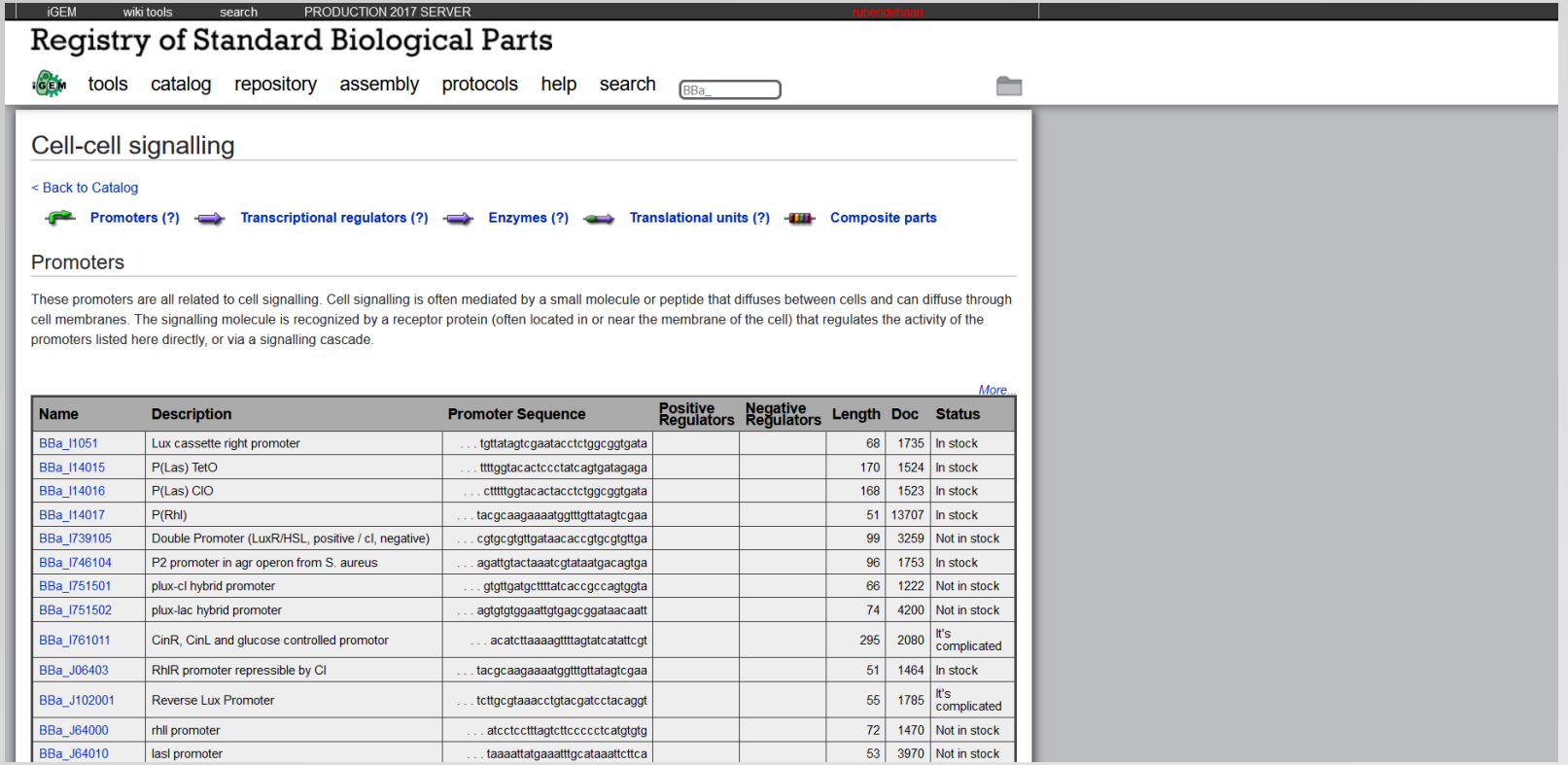
**Situation:**

| | | 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)

# Concept:



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Registry of Standard Biological Parts

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## Cell-cell signalling

< Back to Catalog

Promoters (?) Transcriptional regulators (?) Enzymes (?) Translational units (?) Composite parts

### Promoters

These promoters are all related to cell signalling. Cell signalling is often mediated by a small molecule or peptide that diffuses between cells and can diffuse through cell membranes. The signalling molecule is recognized by a receptor protein (often located in or near the membrane of the cell) that regulates the activity of the promoters listed here directly, or via a signalling cascade.

More...

| Name | Description | Promoter Sequence | Positive Regulators | Negative Regulators | Length | Doc | Status |
|---|---|---|---|---|---|---|---|
| BBa_I1051 | Lux cassette right promoter | . . . tgttatagtcgaatacctctggcggtgata | | | 68 | 1735 | In stock |
| BBa_I14015 | P(Las) TetO | . . . ttttggtacactccctatcagtgatagaga | | | 170 | 1524 | In stock |
| BBa_I14016 | P(Las) CIO | . . . cttttggtacactacctctggcggtgata | | | 168 | 1523 | In stock |
| BBa_I14017 | P(Rhl) | . . . tacgcaagaaaatggtttgttatagtcgaa | | | 51 | 13707 | In stock |
| BBa_I739105 | Double Promoter (LuxR/HSL, positive / cI, negative) | . . . cgtgcgtgttgataacaccgtgcgtgttga | | | 99 | 3259 | Not in stock |
| BBa_I746104 | P2 promoter in agr operon from S. aureus | . . . agattgtactaaatcgtataatgacagtga | | | 96 | 1753 | In stock |
| BBa_I751501 | plux-cI hybrid promoter | . . . gtgttgatgcttttatcaccgccagtggta | | | 66 | 1222 | Not in stock |
| BBa_I751502 | plux-lac hybrid promoter | . . . agtgtgtggaattgtgagcggataacaatt | | | 74 | 4200 | Not in stock |
| BBa_I761011 | CinR, CinL and glucose controlled promotor | . . . acatcttaaaagttttagtatcatattcgt | | | 295 | 2080 | It's complicated |
| BBa_J06403 | RhlR promoter repressible by CI | . . . tacgcaagaaaatggtttgttatagtcgaa | | | 51 | 1464 | In stock |
| BBa_J102001 | Reverse Lux Promoter | . . . tcttgcgtaaacctgtacgatcctacaggt | | | 55 | 1785 | It's complicated |
| BBa_J64000 | rhlI promoter | . . . atcctcctttagtcttccccctcatgtgtg | | | 72 | 1470 | Not in stock |
| BBa_J64010 | lasI promoter | . . . taaaattatgaaatttgcataaattcttca | | | 53 | 3970 | Not in stock |

Source: iGEM parts catalogue (www.parts.IGEM.org, 2021)

## Conclusion:

In the current iGerm.org Cell-to-Cell signalling library a suitable substitute protein for the IL7Rα monomer could not be found. Further research and experimentation could lead to modified proteins that might serve as a substitute for SCID patients lacking IL7Rα.

## 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