

Neonatal screening for PID

- T cell defects (SCID)
- B cell defects (XLA)
- Phagocytic disorders (CGD)
- Complement defects (C2, P)

Genetic causes of SCID

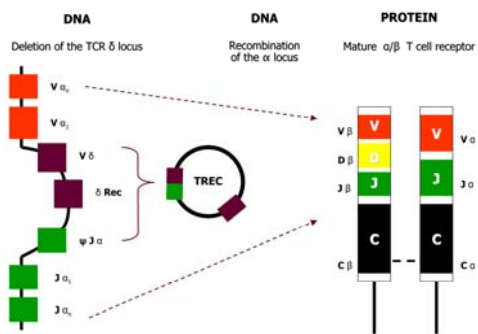
- IL2RG
- IL7RA
- JAK3
- PTPRC
- RAG1/2
- Artemis
- CORO1A
- PRKDC
- ADA
- AK2

Neonatal screening for PID

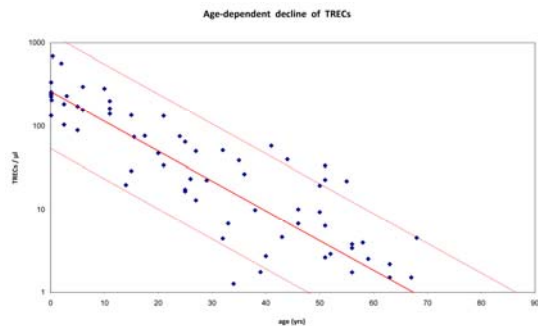
- TRECS (Puck et al 2005)*
- KRECS (Nakagawa et al 2011)

* T cell lymphopenia

Rearrangement of T cell receptor genes



TRECs represent newly formed T cells



TREC screening (for PID)

- Wisconsin 2008*
- Massachusetts 2009
- Louisiana 2009
- New York 2009
- California 2010
- Puerto Rico 2010
- Texas 2010
- Pennsylvania 2010

* Routes and Verbsky

USA update

- 3 030 083 children screened
- 1 265 (0.04 %) FACS referrals
- 52 children with SCID (1/58 000)
- 92 % survival after therapy
- No SCID patient missed
- 460 additional positive samples

Kwan et al, JAMA 2014

Neonatal screening for PID

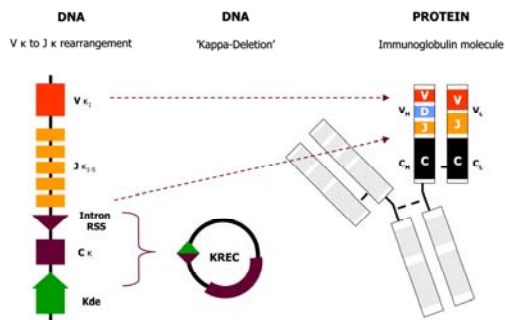
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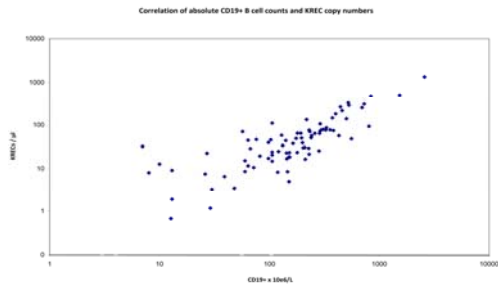
- TRECS (Puck et al 2005)
- KRECS (Nakagawa et al 2011)*

* B cell lymphopenia

Formation of the B cell receptor (BCR)



KRECs represent newly formed B cells

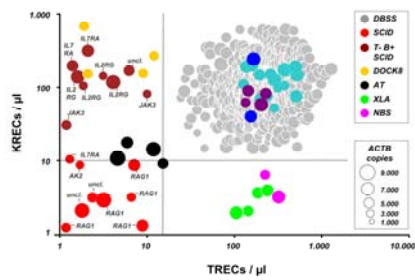


Neonatal screening for PID

- TRECS (Puck et al 2005)
- KRECS (Nakagawa et al 2011)
- β -actin

Borte et al, Blood 2012

Proof of principle (retrospective)



Borte et al, Ann NY Acad Sci 2013

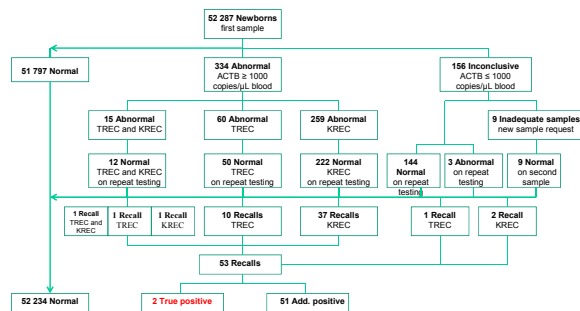
Neonatal screening in Sweden



Time schedule (Sweden)

- 2010 (2 500 anonymous samples)
- 2011 (2 500 anonymous samples)
- 2012 (5 000 anonymous samples)
- 2013-14 (30 000 samples)
- 2014-15 (30 000 samples)
- 2015-16 (30 000 samples)
- 2016 national implementation (?)

Prospective NBS screening (Sweden)

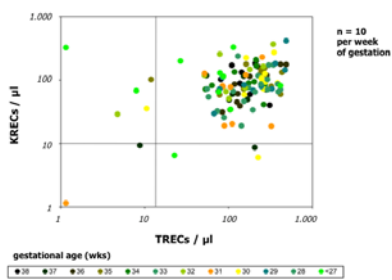


USA update
(non-SCID T cell lymphopenia)

- 29 Prematurity (only)
- 58 DiGeorge
- 21 Trisomy 21
- 4 AT
- 1 Nijmegen Breakage Syndrome
- 117 Secondary T-cell impairment
- 230 "Other"

Kwan et al, JAMA 2014

Additional positive samples - prematurity



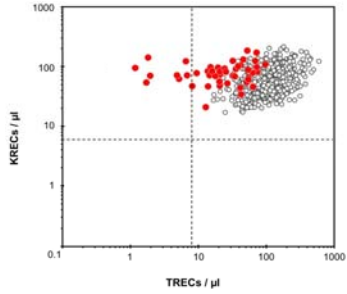
Borte et al, Ann NY Acad Sci 2013

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Kwan et al, JAMA 2014

Additional positive samples - DiGeorge



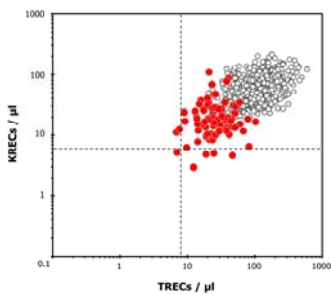
Lingman-Framme et al, JoCI 2014

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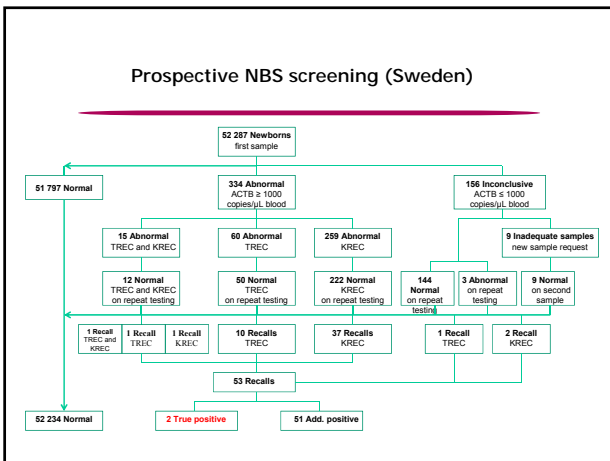
Kwan et al, JAMA 2014

Additional positive samples - Trisomy 21



Verstegen et al, JACI 2014

Prospective NBS screening (Sweden)



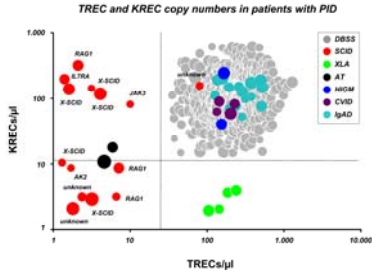
Clinical follow up

- Doctors visit
- Clinical chemistry
- FACS (EuroFlow)
- Genetic testing
 - PID screening panel (219 genes, 2800 exons)
 - Exome sequencing
 - Whole genome sequencing

Future NBS challenges

- "Normal" TREC/KREC SCIDs
- Improved assay performance
- Cut-offs for TREC/KREC
- Granulocyte deficiencies
- Complement deficiencies

Unknown SCID

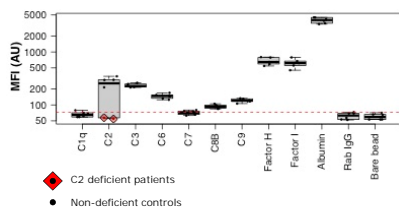


Borte et al, unpublished

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Towards neonatal complement screening



Luminex based assay

Hamsten et al, J Proteomics 2015

Acknowledgements

- Patient referrals

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- TREC assay

Jack Routes, James Verbsky, Jennifer Puck

- Complement assay

Lennart Truedsson, Lillemor Skattum, Peter Nilsson, Maja Nelman

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