Great Ormond Street Hospital for Children NHS Trust

Newborn screening for SCID

European Parliament Brussels 2011

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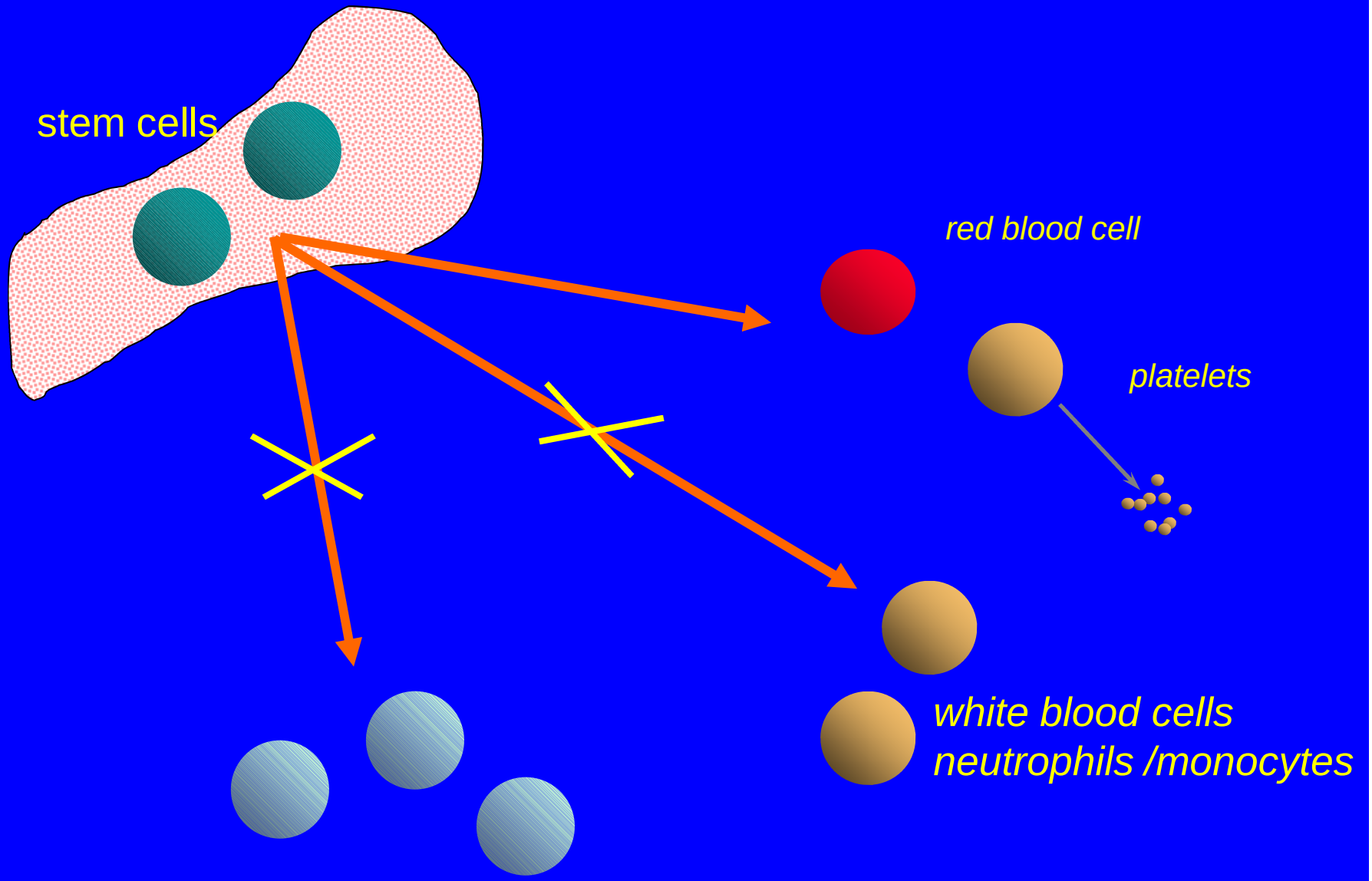
Centre for Immunodeficiency

UCL Institute of Child Health/Great Ormond Street NHS Trust

Primary Immunodeficiency

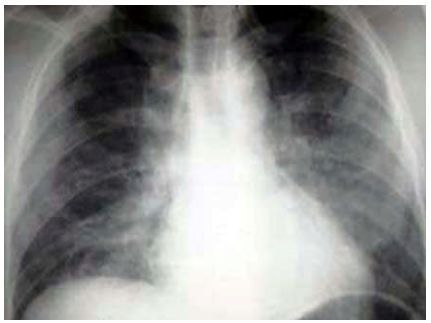


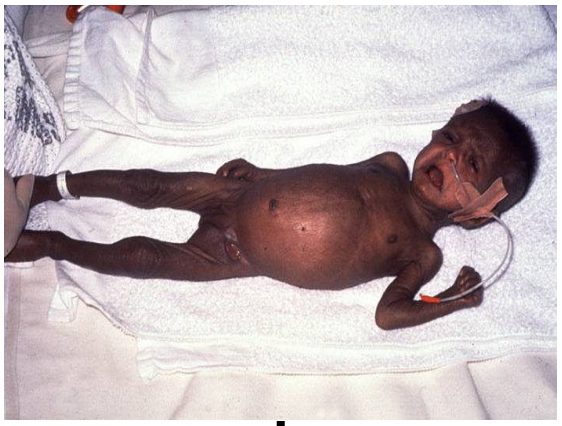
Severe combined immunodeficiency (SCID)

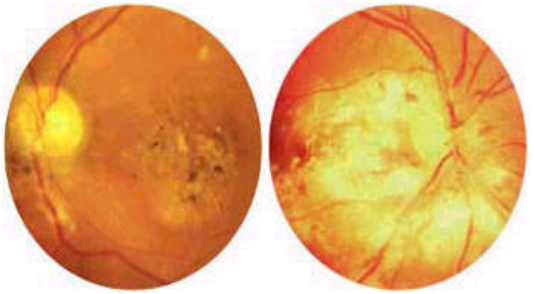
Bacteria

Virus

Fungi



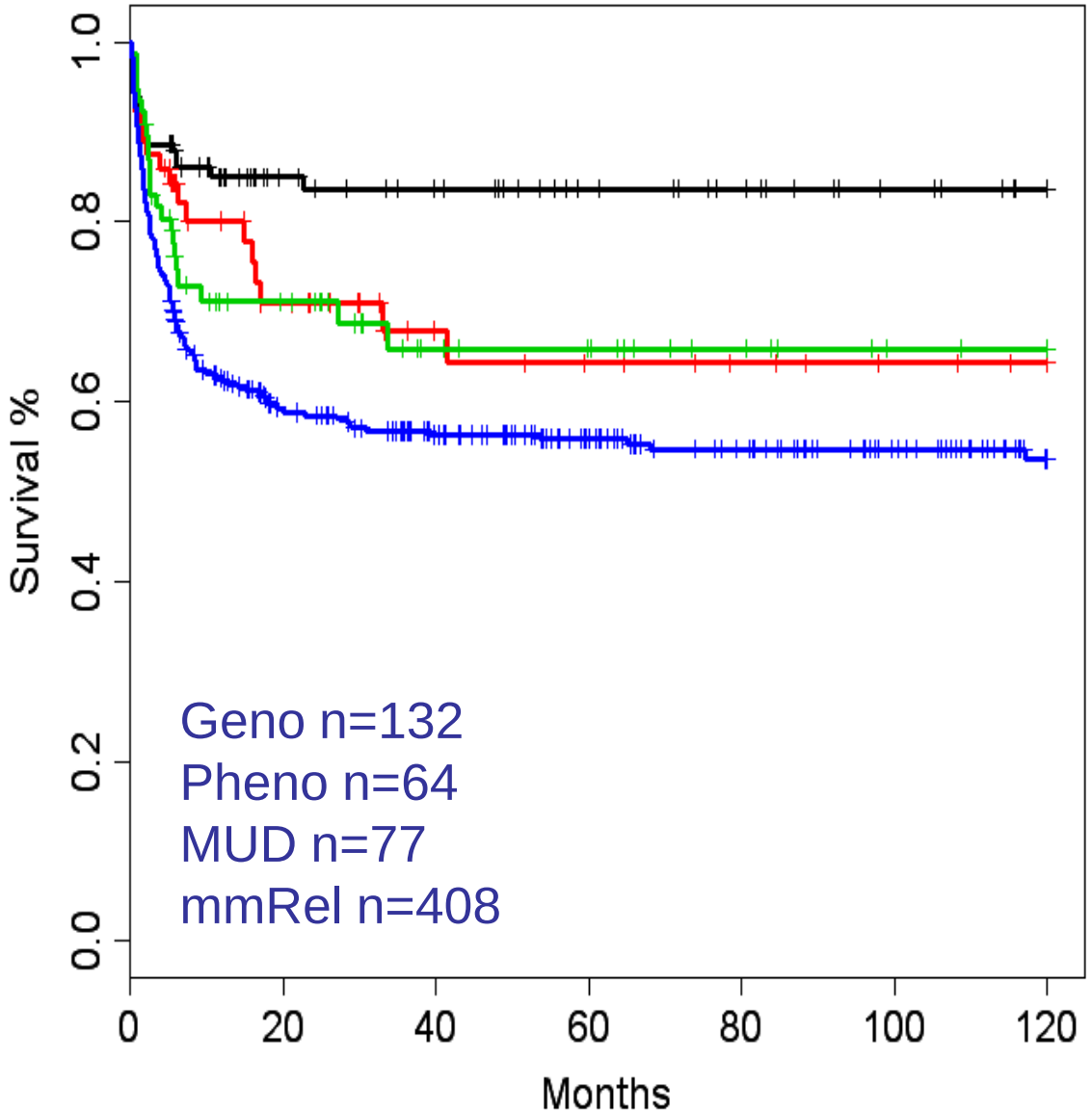




Pneumonia, diarrhoea, repeated infections

SCID children die in first year of life without treatment

Probability of survival in SCID patients after HSCT according to donor-recipient compatibility



10 years Survival rate

Geno : 84%

Pheno : 64%

MUD : 66%

mmRel : 54%

p<0.0001

Factors affecting outcome of transplant in SCID

	Univariate analysis				Multivariate analysis	
	Patients	Deaths	3-year survival, % (95% CI)	p	Hazard ratio (95% CI)	p
After HLA-identical transplantation						
Age at transplantation (months)						
<6	92	12	85 (77–93)	0·0004	1	..
6–11	50	12	73 (59–86)		2·2 (0·9–5·6)	0·12
⩾12	31	14	53 (35–71)		8·3 (2·7–25·4)	0·0002
Prophylaxis*						
Yes	93	14	79 (72–87)	0·024	1	
No	35	12	62 (47–78)		3·9 (1·7–9·3)	0·002
After related HLA-mismatched transplantation						
SCID phenotype						
B(+)	159	53	64 (57–72)	0·0001	1	
B(–)	107	65	36 (26–45)		2·0 (1·3–2·9)	0·0007
Protected environment						
Yes	258	104	57 (50–63)	0·0001	1	
No	20	17	15 (1–30)		5·1 (3·0–8·8)	0·0001
Pulmonary infection (before transplant)						
No	151	58	59 (51–67)		1	
Yes	106	61	38 (28–48)	0·004	2·2 (1·5–3·2)	0·0001

*Trimethoprim-sulfamethoxazole.

Antoine et al Lancet 2003; 361:553-60

Comparison of outcomes in families with SCID

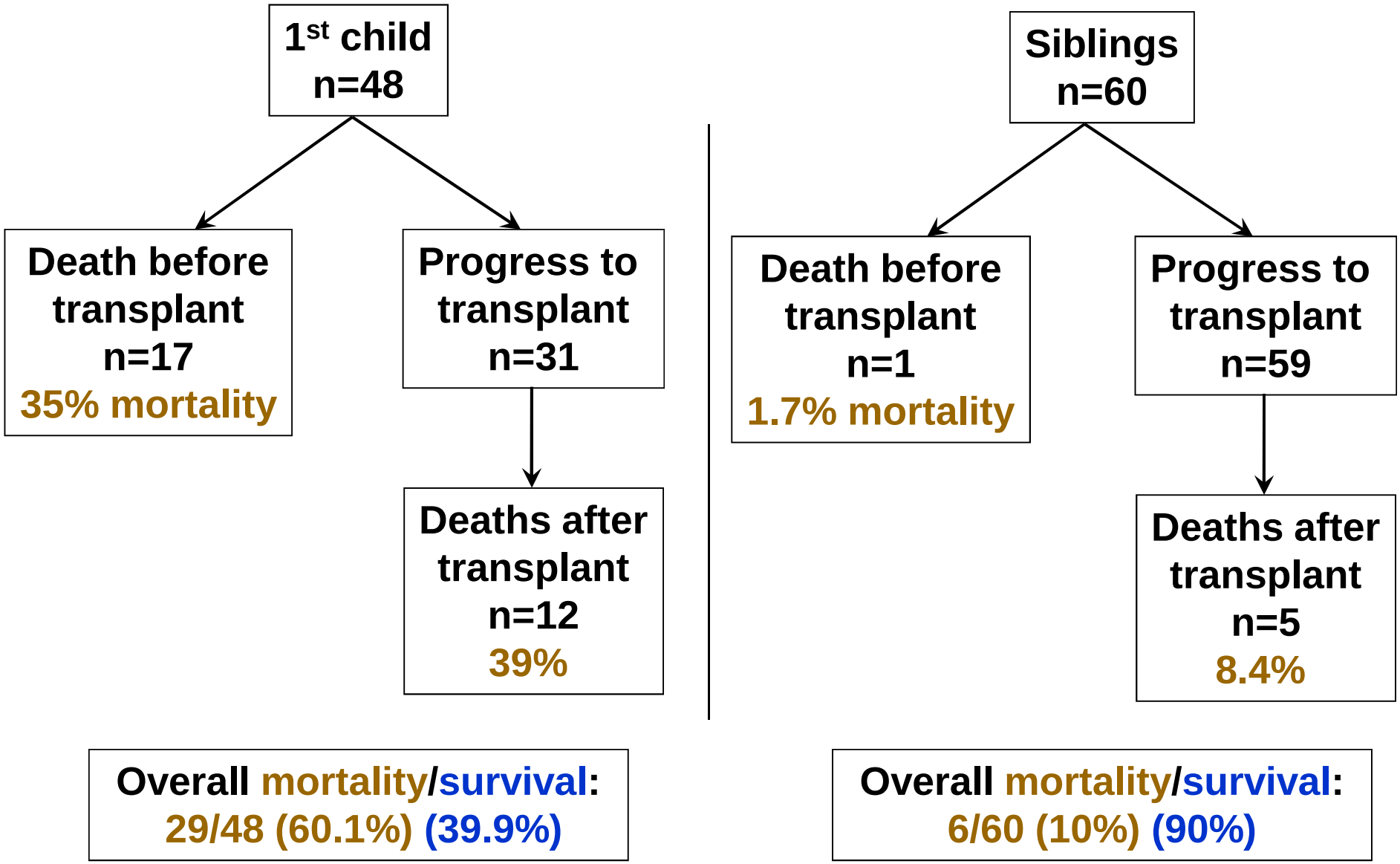
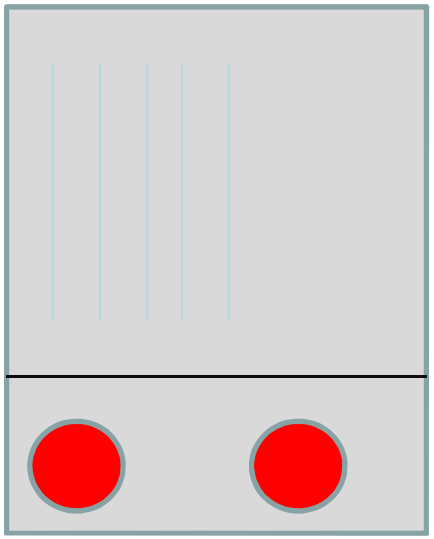
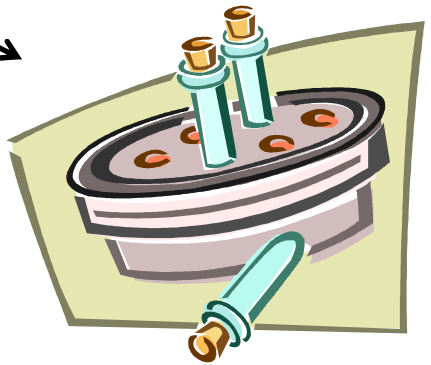


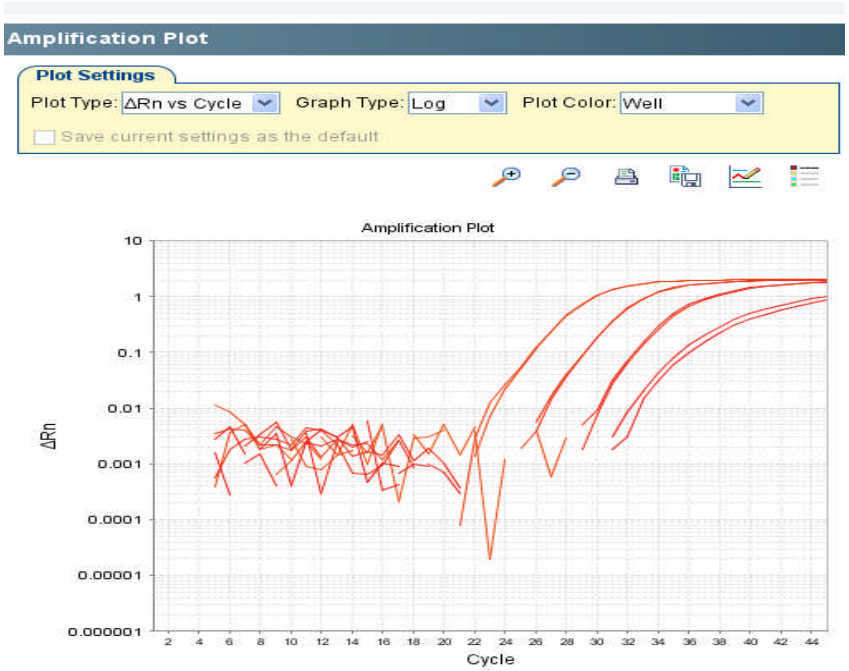
Diagram of process



Guthrie Card



DNA Extraction



Quantitation of TRECs by Real-time PCR

Results of TREC test in known SCID

	Patient	Diagnosis	TRECs per million cells
	MD	SCID ADA Deficiency	0
	SR	SCID X-linked	0
*	LV	CID	0
	JH	Gamma Chain SCID	0
	LR	SCID T low B+ NK+	0
	MH	SCID T low NK+ B+ IL-7 R def.	0
	SC	Gamma Chain SCID	0
	HB	Gamma Chain SCID	0
	AA	SCID T low NK+ B low	0
	NL	Gamma Chain SCID	0
	OC	Gamma Chain SCID	0
	MM	Gamma Chain SCID	0
	TA	RAG SCID	0
	ZK	SCID T- B- NK+	0
*	AC	Evans CID	0
	RR	Gamma Chain SCID	0
	IM	SCID ADA Deficiency	0
*	JA	Gamma Chain SCID	0
	MH	SCID ADA Deficiency	0
	MD	?ADA SCID	0

All SCID DBS TREC samples are zero

Includes patients with maternal engraftment and atypical features

In May 21, 2010, Secretary of Health and Human Services (HHS) announced the addition of SCID – to the core panel of 29 genetic disorders

Economics of screening

- Screening test cost ~ $5 USD (3.5 EUROS)
- Screening all live births in UK (700,000 per year) ~ 2.5m euros

- Undiagnosed SCID patients v costly to health system
- Require long in patient stay, PICU admission, expensive drug courses

- Newborn screening allows early diagnosis, simple preventative measure
- Newborn transplants are simpler, less complicated and require less inpatient stay

- Outcomes for transplant allow treated children to play a full role in society

Summary

- Newborn diagnosis of SCID clearly saves lives
- Reliable assays now available for newborn screening
- Assays and rationale are economically viable
- Impact on both QoL and healthcare burden make a strong argument for universal NBS for SCID