

# ELUNDISIIRDAMISED EILE, TÄNA, HOMME

Peeter Dmitriev  
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# Püha Cosmas ja Damian



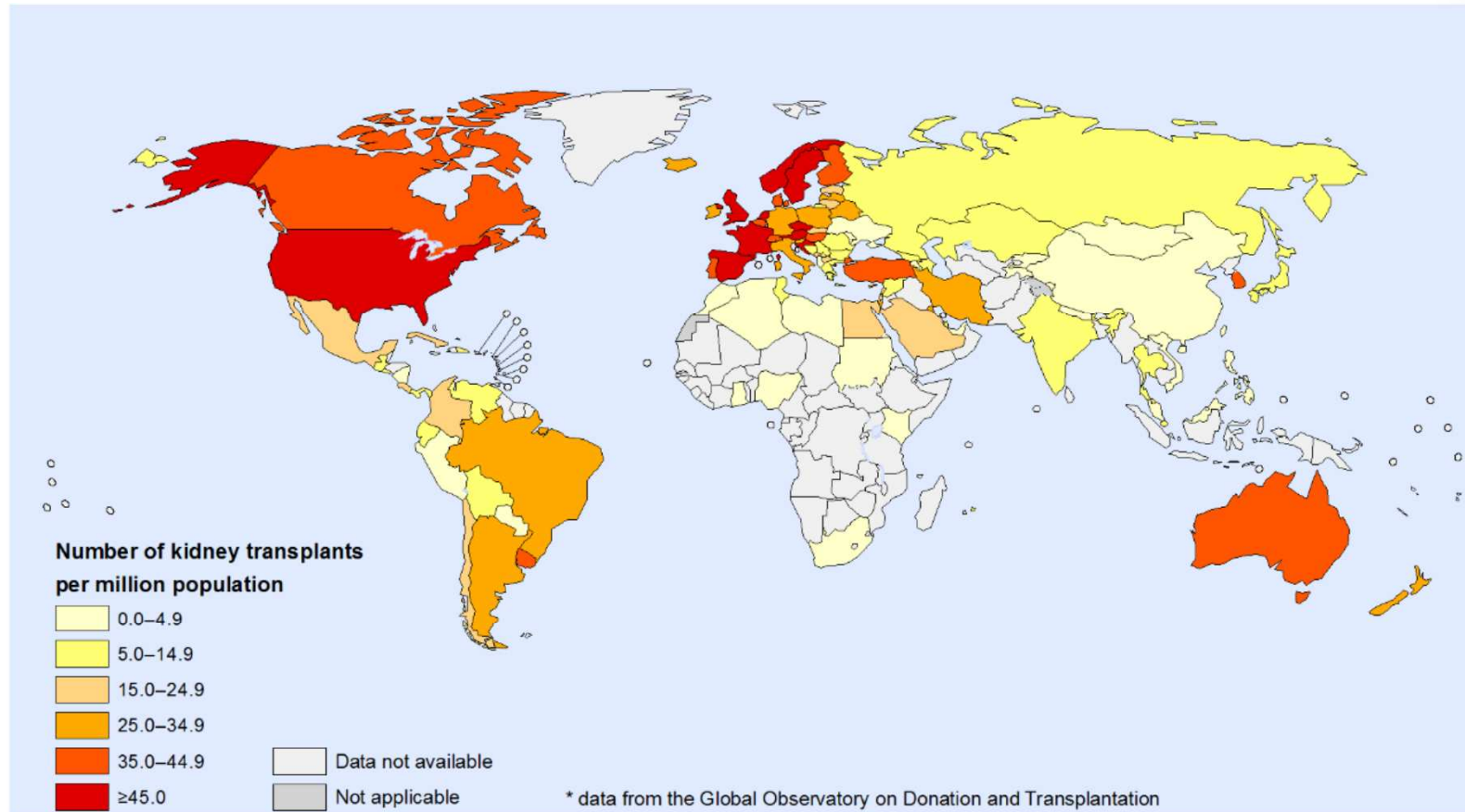
## Gustav Simon (1824-1876)



# Юрий Вороной(1895-1961)



# Neerusiirdamised maailmas 2014



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Data Source: Global Observatory on Donation & Transplantation. Map Production: Information Evidence and Research (IER)  
World Health Organization



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**Table 1.** Common side effects of main immunosuppressive drugs.

	Medication	Side Effects
Medication used for maintenance therapy	Calcineurin inhibitors (CNI)	Nephrotoxicity, neurotoxicity, hypertension, hyperlipidemia and hyperkalemia, diabetes mellitus, increased bone resorption, hirsutism, gingival hyperplasia, hearing impairment and cholestatic syndrome, post-transplant malignancies and skin cancers
	Azathioprine	Hepatic nodular hyperplasia, portal sclerosis, myelosuppression, post-transplant malignancies and skin cancers
	Mycophenolate	GI disturbance, myelosuppression growth retardation
	Corticosteroids	Cushingoid appearance, fluid retention, diabetes mellitus, hypertension, growth impairment, hyperlipidemia, osteopenia, impairment in wound healing, failure to thrive
Medication used for induction therapy	Anti-CD25 receptor antibodies (basiliximab, daclizumab)	Anaphylaxis, allergic reaction
	Anti-CD52 monoclonal antibody (alemtuzumab)	Profound lymphocyte depletion, which increases the risk of infection, in particular CMV reactivation
	Antithymocyte globulin (ATG)	Lymphopenia, serum sickness, anaphylactic reaction, shock, bronchospasm

# Aktuaalsed strateegiad

- Dooside vähendamine, konversioon jne
- Mitte-nefrotoksilised ained
- Tolerantsus

# Alternatiivid

**Table 2.** Alternatives to full dose drug regimens.

Strategy	Definition	Timing
Minimization	Lower dosage of drug	Planned <i>de novo</i> , or result of adverse event
Conversion	Tapering of drug dose until eliminated and replaced with other immunosuppressant	Usually result of adverse event
Withdrawal	Tapering of drug dose until eliminated, may be replaced with other immunosuppressant	Planned <i>de novo</i> or result of adverse event
Avoidance	No drug given, other immunosuppressant used	Planned <i>de novo</i>



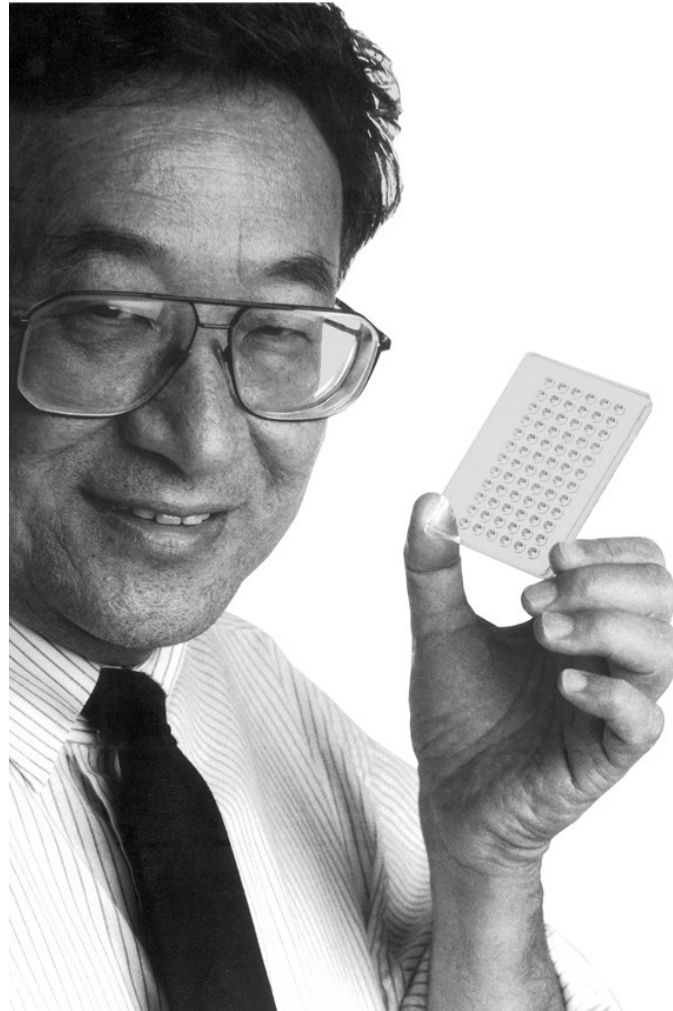
## Uued ravimid

- Belatacept
- Proteiinkinaas C inhibiitorid
- Proteasoomi inhibiitorid
- Rituximab

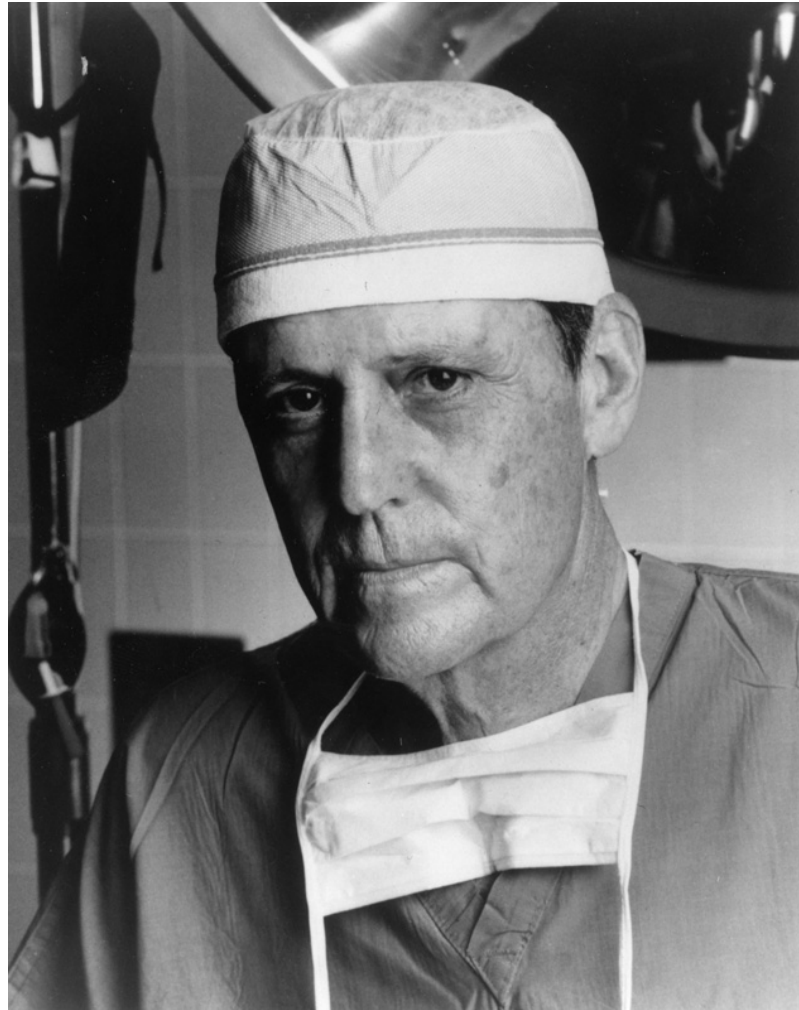
# Tolerantsus

- ~100 patsienti (250 000st)
- „operational“, „prope“, „almost“, „minimal IS“
- Ei ole seost HLAga, äratõugetega, doonoriga vms
- Immunokompetentne seisund
- Ajas metastabiilne

# Paul Terasaki (1929-2016)



# Thomas Starzl (1926-2017)



## Colorado 1962-1963

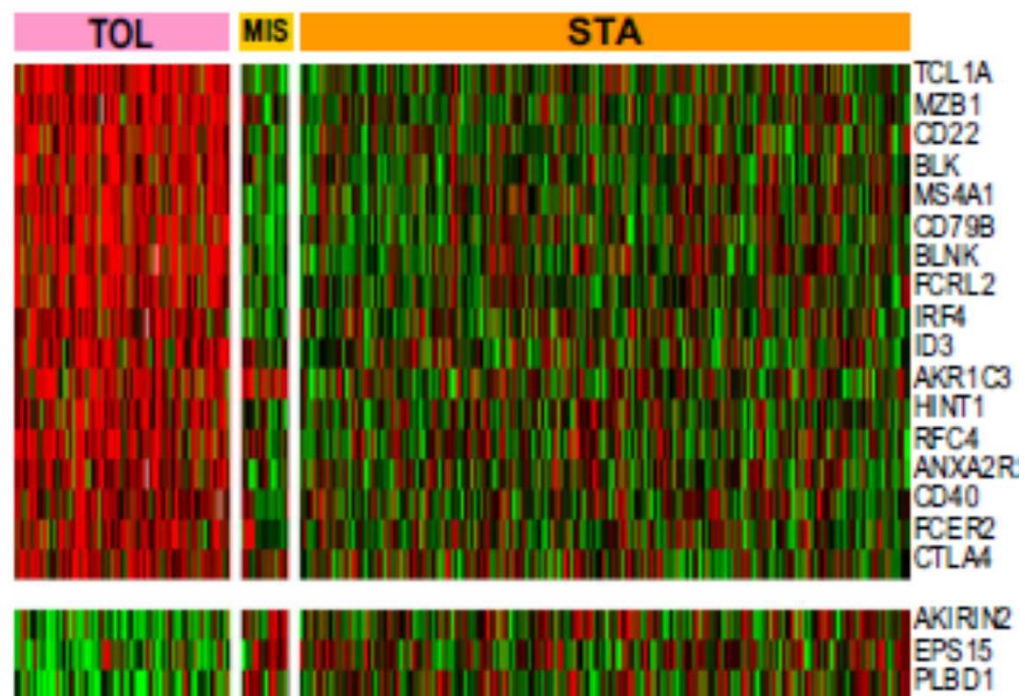
- 46 elusdoonori neeru siirdamist
- Asatiopriin 2 nädalat enne siirdamist monoterapiana
- Prednisoloon ainult äratõukel
- 9 patsienti < 40a
- 7 patsienti tolerantsed 3-38a
- Keegi pole suutnud korrata

## Tolerantsuse tuvastamine

- **Immune Tolerance Network (ITN) – USA**
- **Indices of Tolerance (IOT) – Euroopa**
- **Reprogramming the immune System for the Establishment of Tolerance (RISET) - Euroopa**

# Tolerantsus

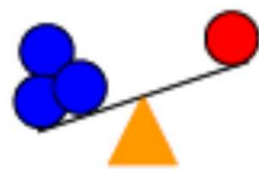
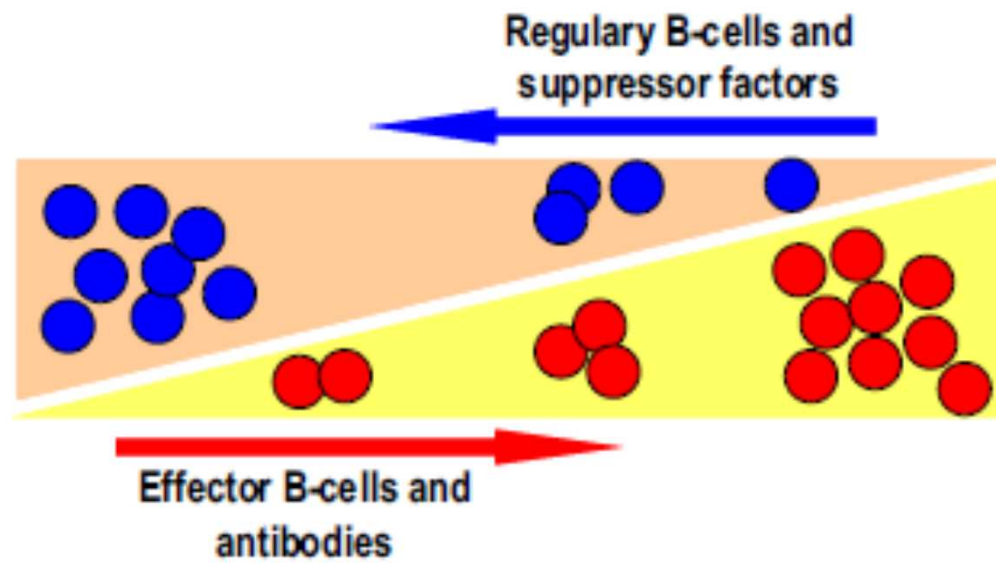
- Eriline B raku geenisignatuur
- Tolerantsuse tuvastamine ja jälgimine
- IS retsipientide monitooring



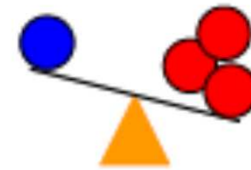


## Regulatoorsed B rakud (Breg)

- IL-10, TGF- $\beta$ , GrB
- Kas B rakud on osalised tolerantsuse säilimisel (mitte tekkimisel) või nad on tolerantsuse peegeldus?



Tolerance



Rejection

# Tolerantsus

- IS foonil vajalik aeg – 10 aastat
- Neer 5-7%
- Maks > 60%

# Regulated T cells (Treg)

**Table 1.** Published studies that have investigated Treg therapy in humans.

Disease	Number of patients	Total number of Treg infused	Main results	References
GvHD after HSCT	2	$1 \times 10^5 - 3 \times 10^6/\text{kg bw}$	<ol style="list-style-type: none"> <li>1. Discontinuation of immunosuppression in patient with chronic GvHD</li> <li>2. Slowing of pace of clinical deterioration in patient with acute GvHD</li> </ol>	[18]
Prevention of GvHD after HSCT	23	$1-30 \times 10^5/\text{kg bw}$	Reduction in acute GvHD (grade 1–2) compared with historical controls	[31]
Prevention of GvHD after HSCT	28	$2-4 \times 10^6/\text{kg bw}$ (unexpanded)	<ol style="list-style-type: none"> <li>1. Acute GvHD (<math>\geq</math> grade 2) in only two of 28 patients</li> <li>2. No chronic GvHD</li> </ol>	[32]
Early onset Type 1 DM	10	$10-20 \times 10^6/\text{kg bw}$	<ol style="list-style-type: none"> <li>1. Less insulin requirement in treated versus non-treated patients</li> <li>2. Higher C-peptide levels in treated versus non-treated patients</li> </ol>	[33]

Bw, bodyweight; DM, diabetes mellitus; GvHD, graft-versus-host disease; HSCT, haematopoietic stem cell transplantation.

# Treg elundisiirdamisel

**The ONE Study** (A Unified Approach to Evaluating Cellular Immunotherapy in Solid Organ Transplantation)

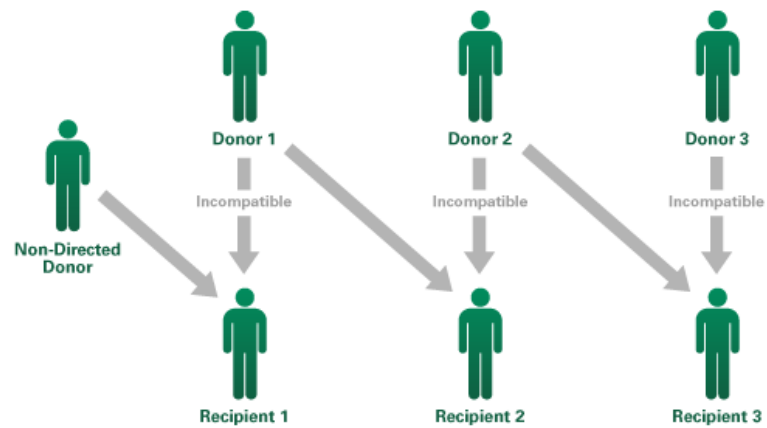
al. 2014 – Oxford, London, Berliin, Boston, San Francisco

- Autoloogsed Treg LRD Tx
- 3-5 päeva pärast siirdamist
- Eesmärk – GMP/ohutus
- 60 patsienti
- 40 000 eurot

# Perspektiivid

- SOD (superoxide dismutase) ja isheemia-reperfusiooni sündroom
- IdeS endopeptidaas (Immunoglobulin G-degrading enzyme of *S.pyogenes*)

# Kidney Paired Donation



Second Largest Kidney Swap in History



Two Georgia men are part of "Chain 221", the world's second largest kidney swap, and the largest kidney swap to be concluded in less than 40 days. Named "Chain 221" by the National Kidney Registry, the chain involved 56 participants, which facilitated 28 transplants in 19 transplant centers across the U.S., including the Emory Transplant Center.

