Dr Paul Turner

Research Scientist

Dunedin

Will Stem Cells be a Cure for Diabetes? - Main Session

Friday, 21 June 2013 | Start 4:50pm | Duration: 20mins | Baytrust



Spinal Cord Society NZ Inc.

- **Who:** Started by Noela & Keith Vallis & people with spinal cord injury (SCI), their families and care-givers in 1988.
- **Aim:** To support research into treatment of SCI and achieve a "Cure" - Neurological repair and, or regeneration.
- **Strategy:** Initially supported United States SCS.

  Later funded training of a NZ Neuroscientist in USA.

  Set up a Dunedin laboratory & a NZ-based research program!

  Laboratory projects with specific translational research goals.

  Development of clinical studies.

SCSNZ & Regenerative Medicine

- Spinal cord injury is an extremely complex issue.
- Successful treatments will require a combination of approaches including:
  1. Stabilise – prevent further physical/metabolic damage.
  2. Repair & reconstruct – fix and replace .
  3. Physiotherapy – relearn function.

Stem Cell Therapies = adult mesenchymal (stromal) stem cells from bone marrow.

Mesenchymal Stem Cells

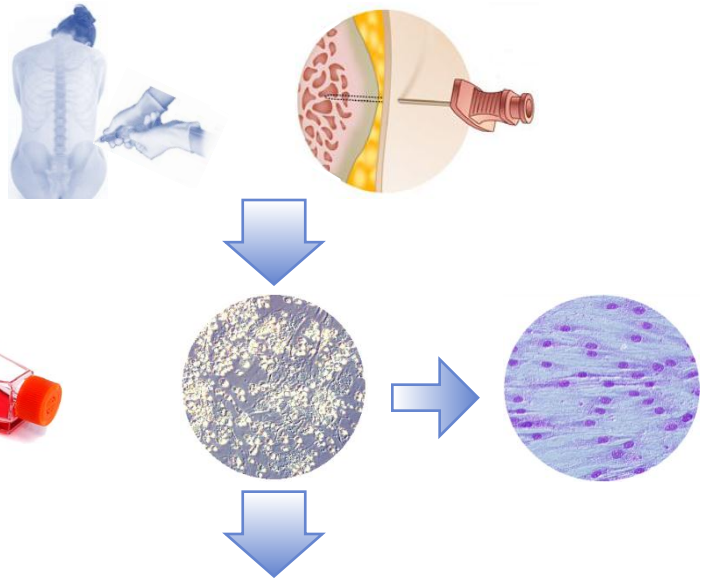
What are they?	• Adult multi-potent stem cells. • Capable of differentiating into mesenchymal tissue (bone, fat, cartilage, smooth muscle, et al). • Repair cell.
Where are they?	• Bone marrow, fat, umbilical cord, many other tissues.
What are their useful properties?	• May be capable of differentiating into other cell types eg. neuronal/ hepatic/ pancreatic. • Homing to sites of injury • Secrete trophic factors. • Immunomodulatory

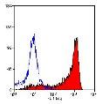
Autologous bone marrow MSCs

Bone marrow aspirate taken

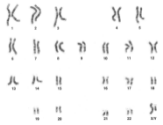
Bone marrow stem cells isolated and grown

Bone marrow stem cells tested for quality and stored frozen for trial

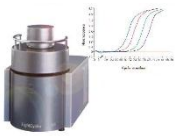




Surface markers

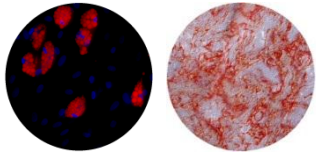


Karyotyping

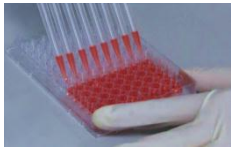


Pathogen screen

Colony forming



Differentiation



Immunosuppression

Clinical trials with stem cells.

- Regulatory details are being worked out worldwide.
- In NZ:
  - Standing Committee On Therapeutic Trials (SCOTT Committee).
  - Ethical approval from HDEC
- Spinal cord injury trials take a long time and measuring benefit is multimodal.
- Strategic decision to target an “easier” disease to get cells into clinical trial = Type-1 diabetes.

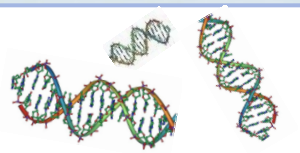
Type-1 Diabetes

A combination of factors.

Autoimmune destruction of insulin producing cells.

Type 1 Diabetes

15,000 NZers, increasing 5%p.a.
Insulin dependent
Devastating long term complications



Genetic background

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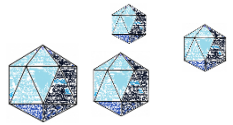
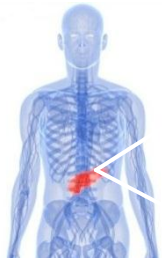
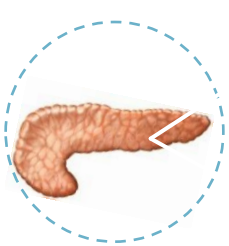
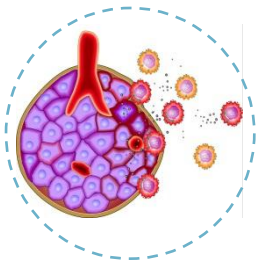


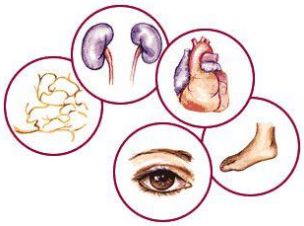
Viral Infection?







Pancreas T-cells destroy islet cells

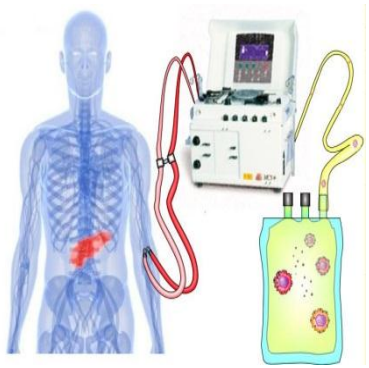


Type-1 diabetes

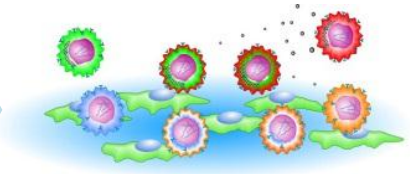
Trial of Zhao et al. 2012, Participants.

• Median age:	29 years, range 15 - 41.
• Median diabetic history:	8 years, range 1 – 21.
• Number of participants:	➢ 15 type-1 diabetics. ➢ 12 treated. ➢ 3 controls .

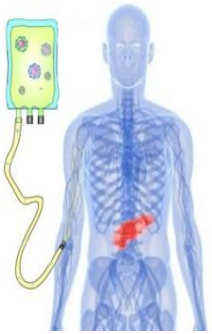
Trial of Zhao et al. 2012, Procedure.



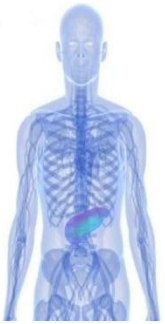
T cells from patient collected.



T cells deactivated by allogeniec umbilical cord blood stem cells *ex vivo*



T cells infused back to patient to protect regenerating islet cells



Patient monitored for changes in diabetes status.

Zhao Y, et al., 2012. Reversal of type 1 diabetes via islet β cell regeneration following immune modulation by cord blood-derived multipotent stem cells. BMC Med. 10:3.

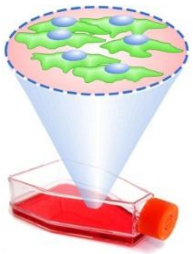
Trial of Zhao et al. 2012. Outcomes

Diabetes severity	(12 weeks post treatment) Severe	Moderate	Control (moderate)
• C-peptide levels	+0.21	+0.42	-0.08
• HbA1c	-1.68	-1.91	-0.30
• Insulin dose	-25%	-38%	0.00
• Markers of immune response	• CD4+CD25+Foxp3+ cells increased (Treg cells) • TGFb levels increased • Restoration of Th1/Th2/Th3 cytokine balance		

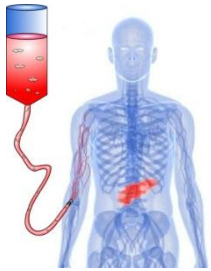
Results suggest autoimmune response was either stopped or attenuated allowing slow islet recovery & insulin production

Proposed trials at SCSNZ

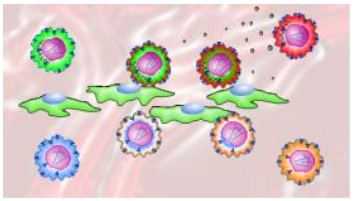
Trial 1



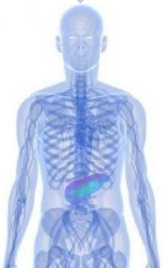
Bone marrow stem cells from patient grown and activated.



Bone marrow stem cells infused into patient.

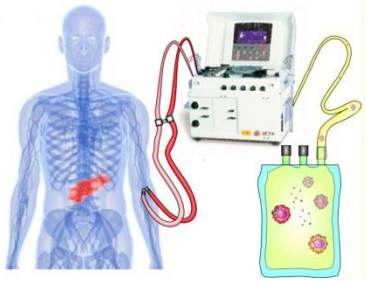


T cells deactivated in patient.

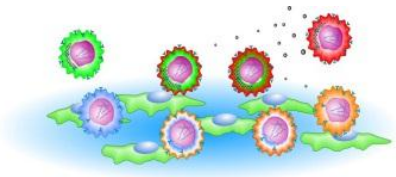


Patient monitored for changes in diabetes status.

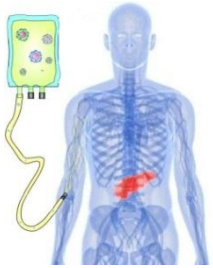
Trial 2



T cells from patient collected.



T cells deactivated by bone marrow stem cells in flask



T cells infused back to patient to protect regenerating islet cells

Parameters to be monitored

Efficacy measures

- C-peptide levels
- HbA1c
- Insulin usage
- Blood glucose level monitoring

Immune measures

- lymphocyte subsets, (CD4, CD8, B, NK)
- IgG, IgA and IgM serum levels.
- Tetanus toxoid antibody, anti-CMV and, or anti-EBV
- Anti-Pneumococcal polysaccharide mix
- CD4+ CD25+ FoxP3 positive lymphocytes.
- T lymphocyte responses against i-IA-2, GAD, Insulin

Project Team

Dr Jim Faed	Haematology/Clinical Trials
Dr Paul Turner	Stem Cell Biology
Dr Sarah Young	Immunology
Prof. Jim Mann	Diabetology
Dr Ben Wheeler	Diabetology