Oral nanotherapeutics for precision targeting of liver antigen presenting cells in type 1 diabetes

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Disclosures

- Director and CEO of Endo Axiom Pty Ltd
  - Endo Axiom leads commercialisation and clinical development of this technology.

ENDO AXIOM

Endo Axiom is focused on prevention of autoimmune diseases and improving the quality of life of diabetics.

We develop biotechnology platforms for the oral delivery of drug and biologics and take these to clinical validation.

Problem: Type 1 Diabetes

- **Type 1 diabetes**
  - Autoimmune disease in childhood
  - 16 yr reduced life expectancy
  - Chronic disease burden
  - 30 bn USD economic cost in the US & 81 bn USD globally

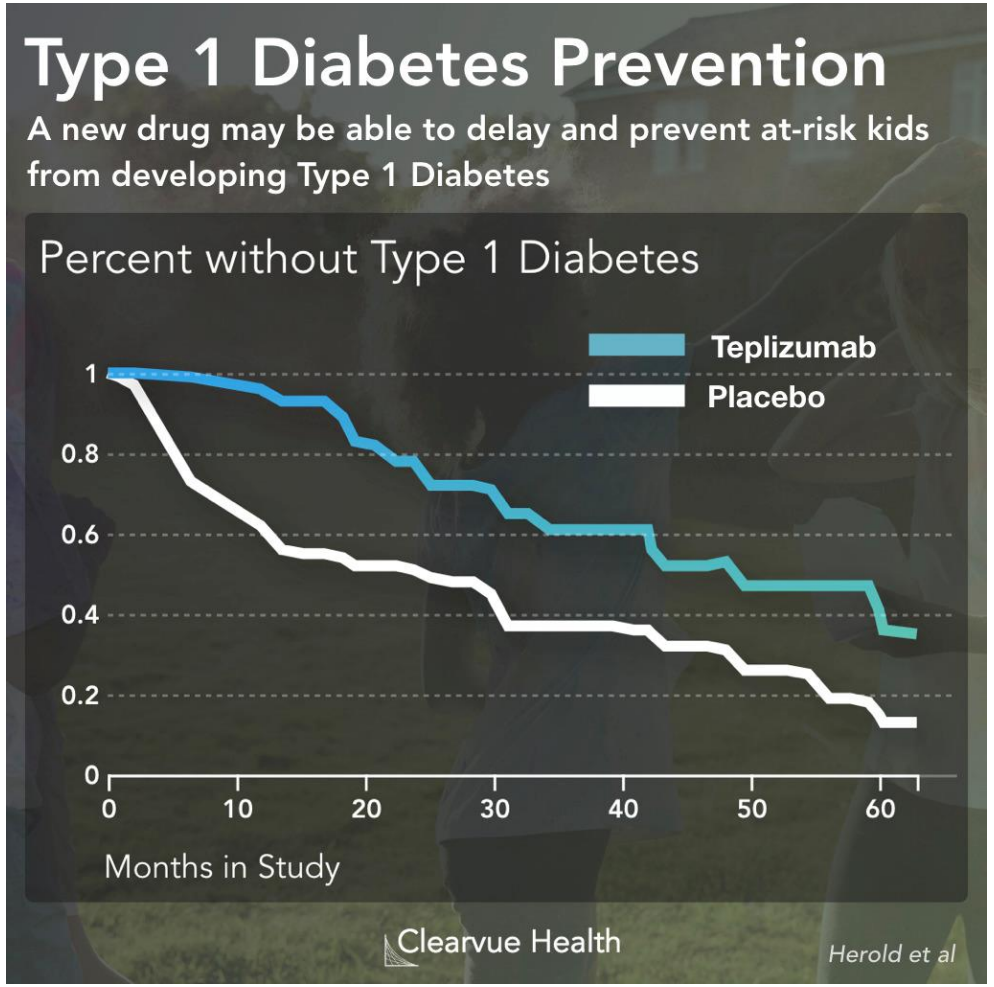
https://www.thejdca.org/publications/report-library/archived-reports/2022-reports/view-this-email-in-your-browser-click-here-to-unsubscribe-the-growing-global-burden-of-t1d.html

Lonergan-Foundation Jdrf Australia Study Report – Insights into Type 1 Diabetes People in Australia.; Australia, 2020.

Modelling the total economic value of novel type 1 diabetes (T1D) therapeutic concepts, January 2020, Health Advances

Problem: Single Preventative Treatment

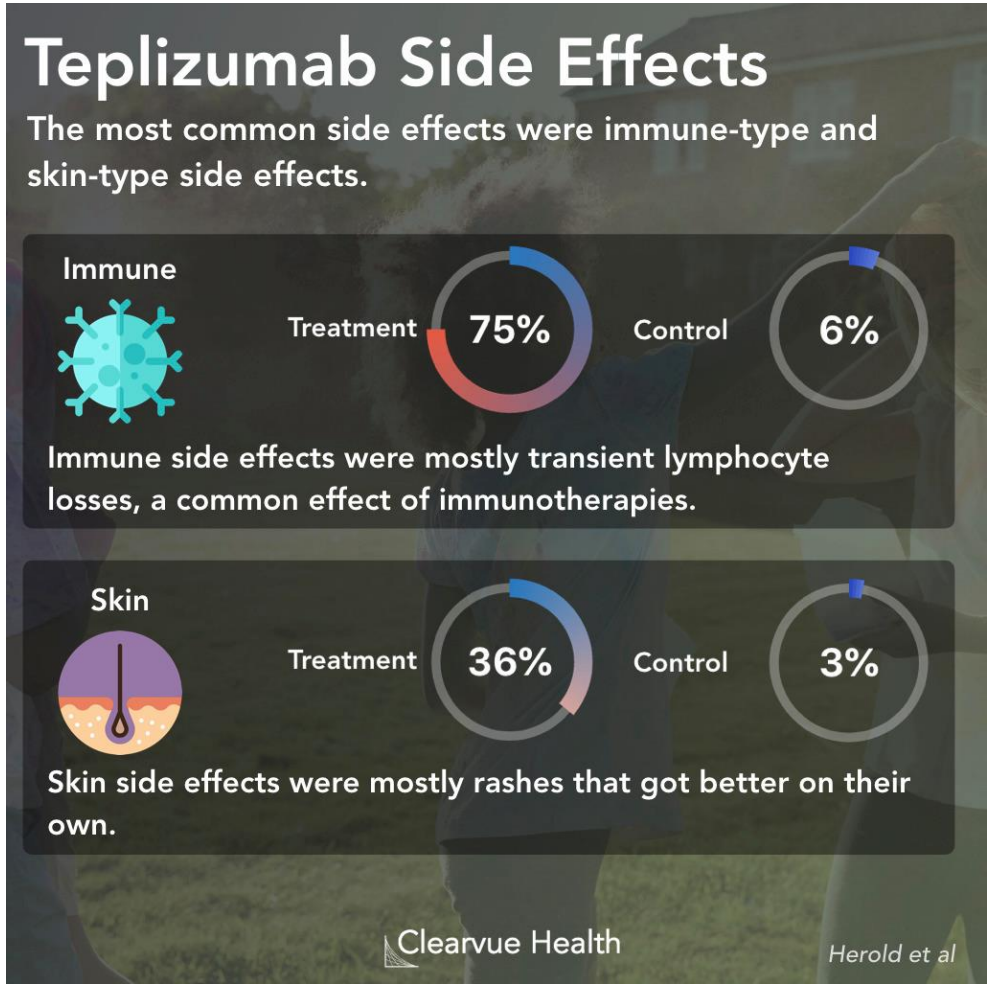
- **Teplizumab**
  - Anti-CD3 monoclonal antibody
  - Delays onset by 3 years
  - Acquired by Sanofi for 2.9 billion USD in 2023



https://www.clearvuehealth.com/b/teplizumab-diabetes-study/

Problem: Immune Suppressive Agent

- **Teplizumab**
  - 70% incidence of leukopenia
  - 30% incidence neutropenia



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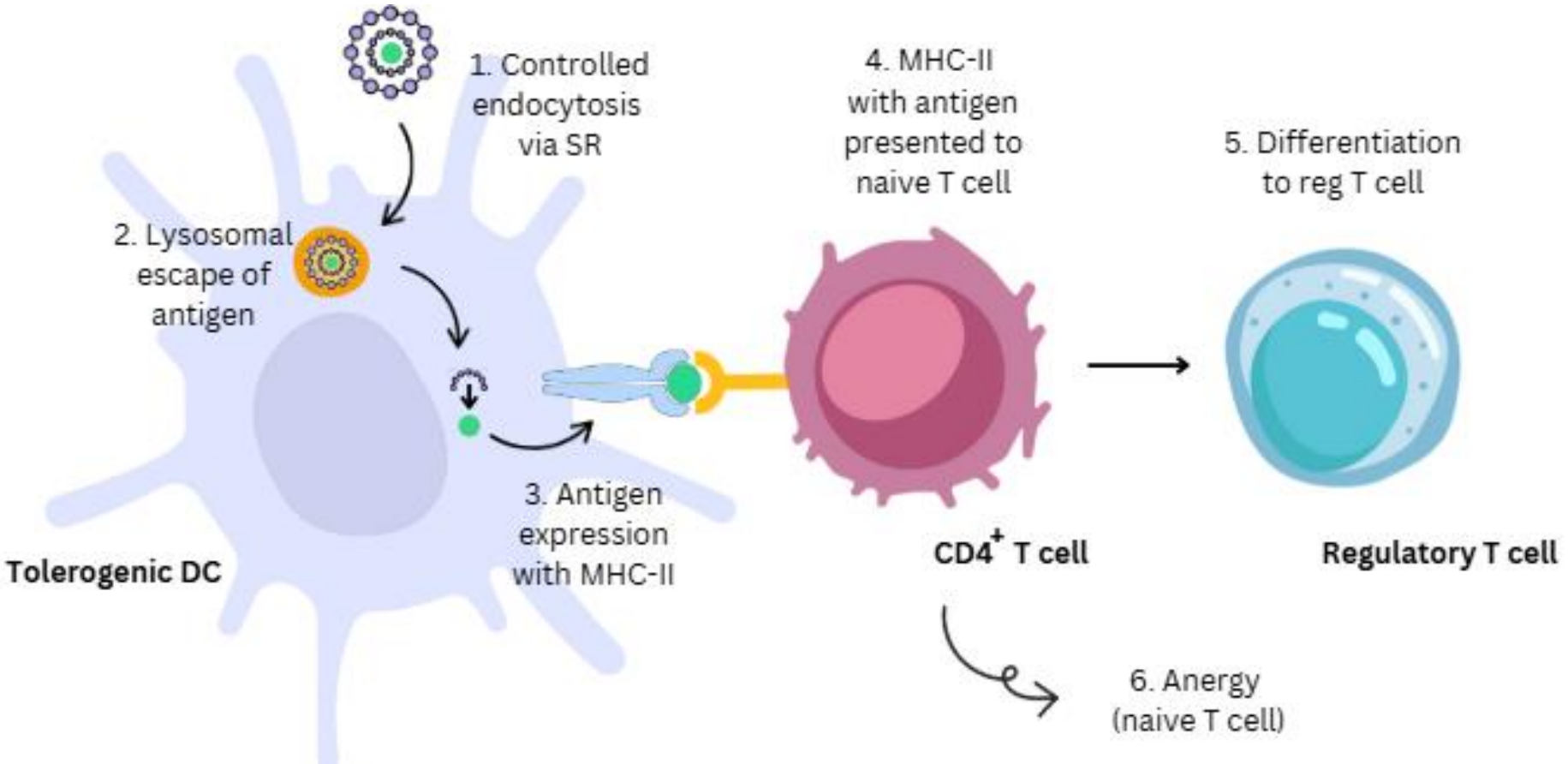
Our Solution: Oral nanotherapeutic to induce tolerance via to antigen presenting cells



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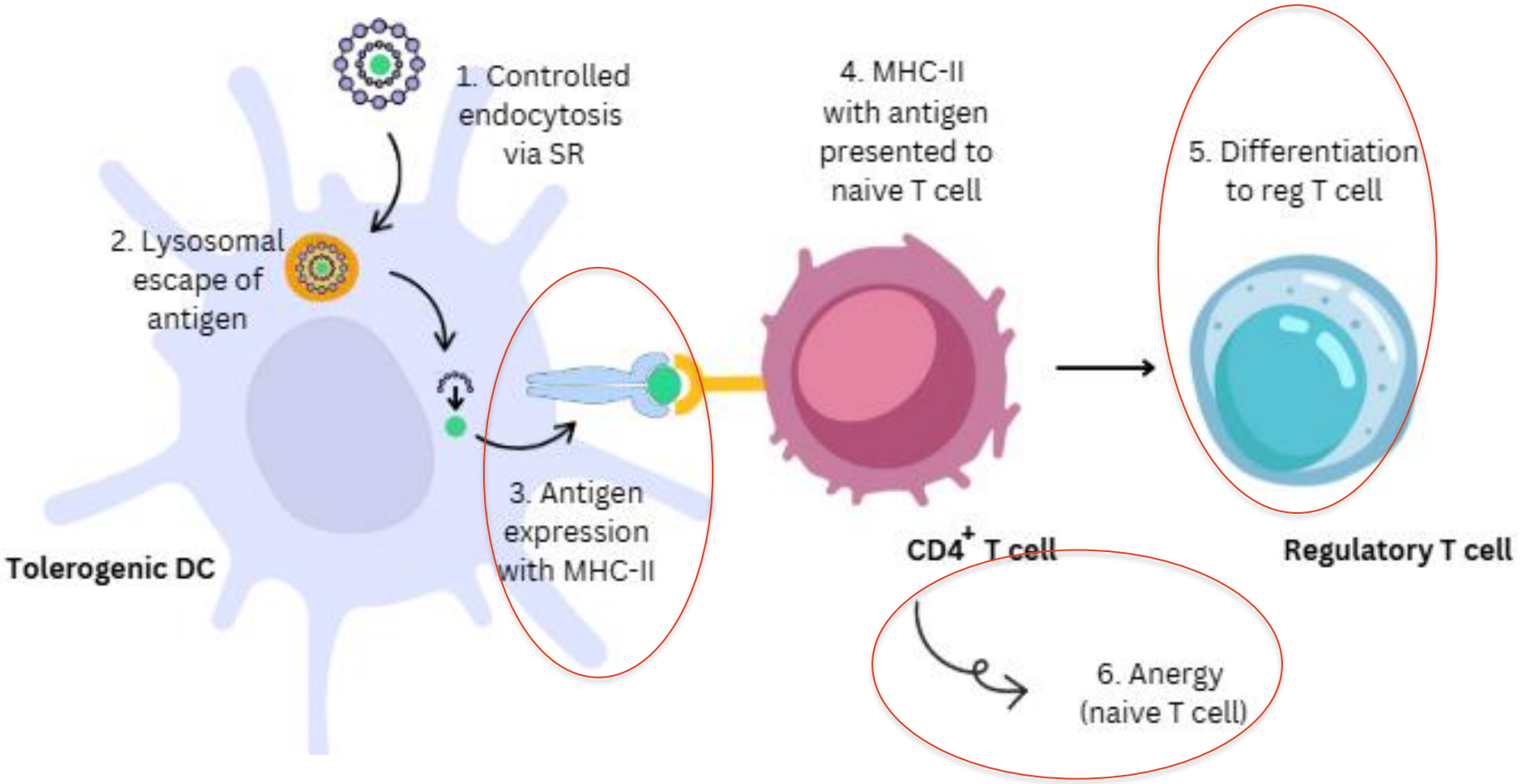
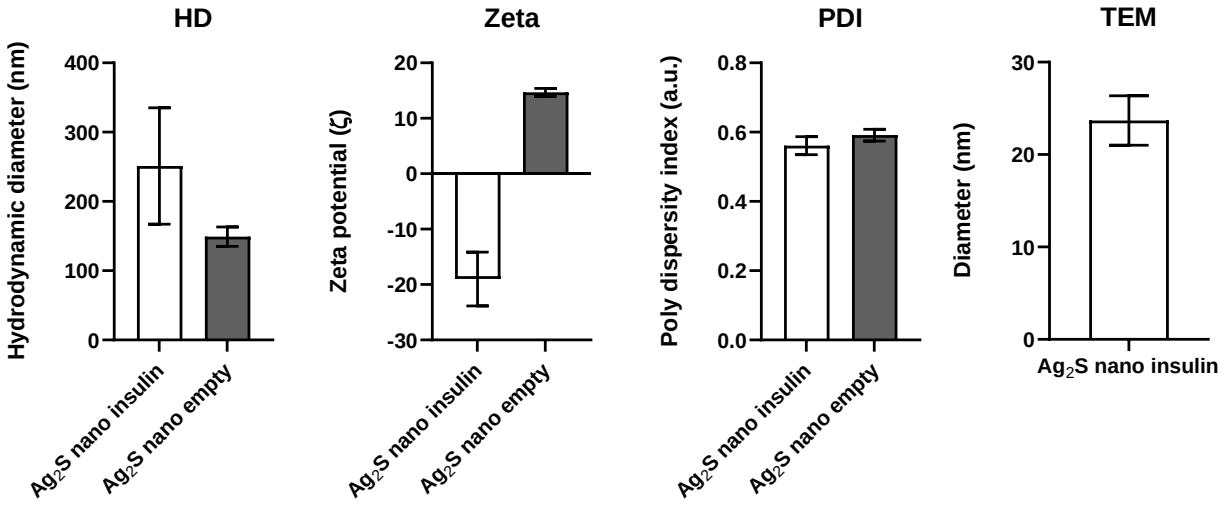
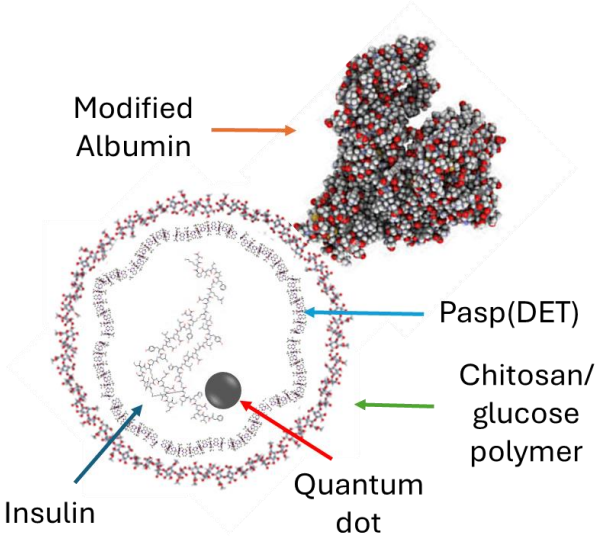
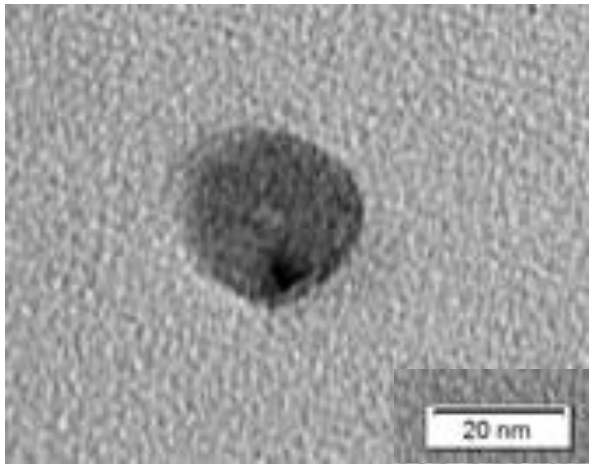


Nano insulin characteristics

- **The complex contains:**
  - Quantum dot core
  - The insulin antigen
  - Lysosome escape polymer
  - Acid resistant polymer
  - A targeting

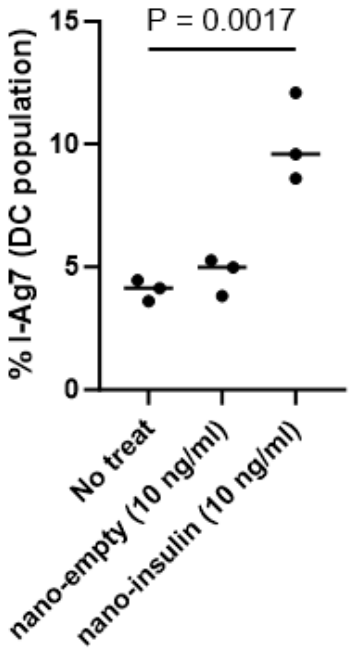




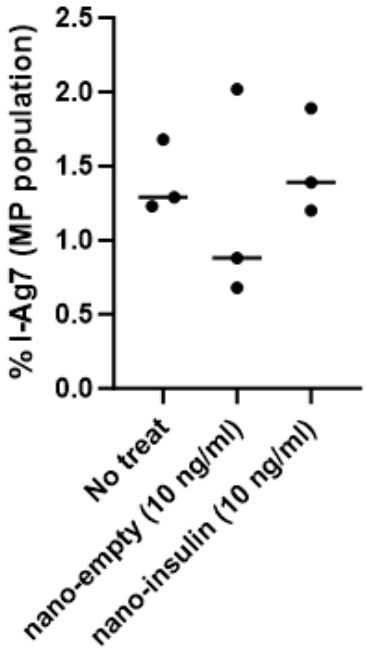


Targets dendritic and endothelial cells in the liver and expresses insulin antigen with MHCII

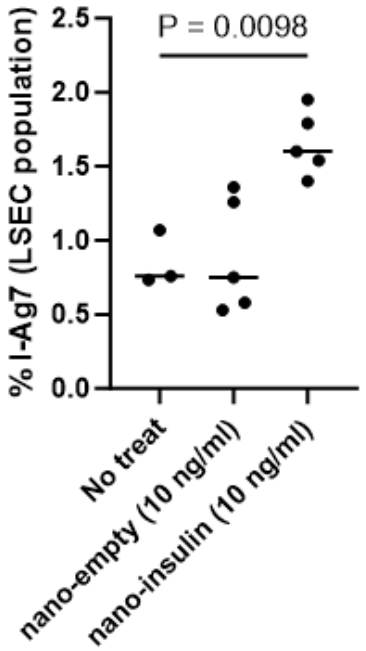
Dendritic cell



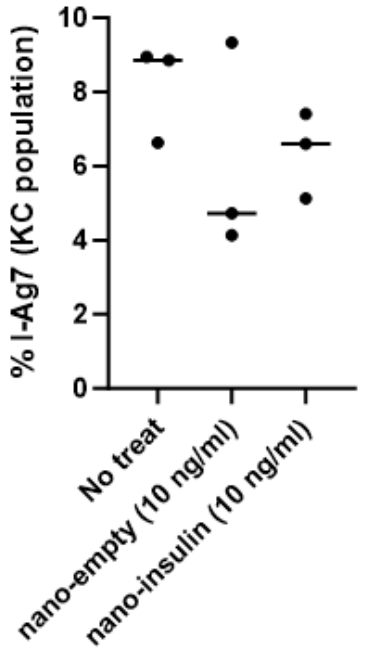
Macrophage



Endothelium

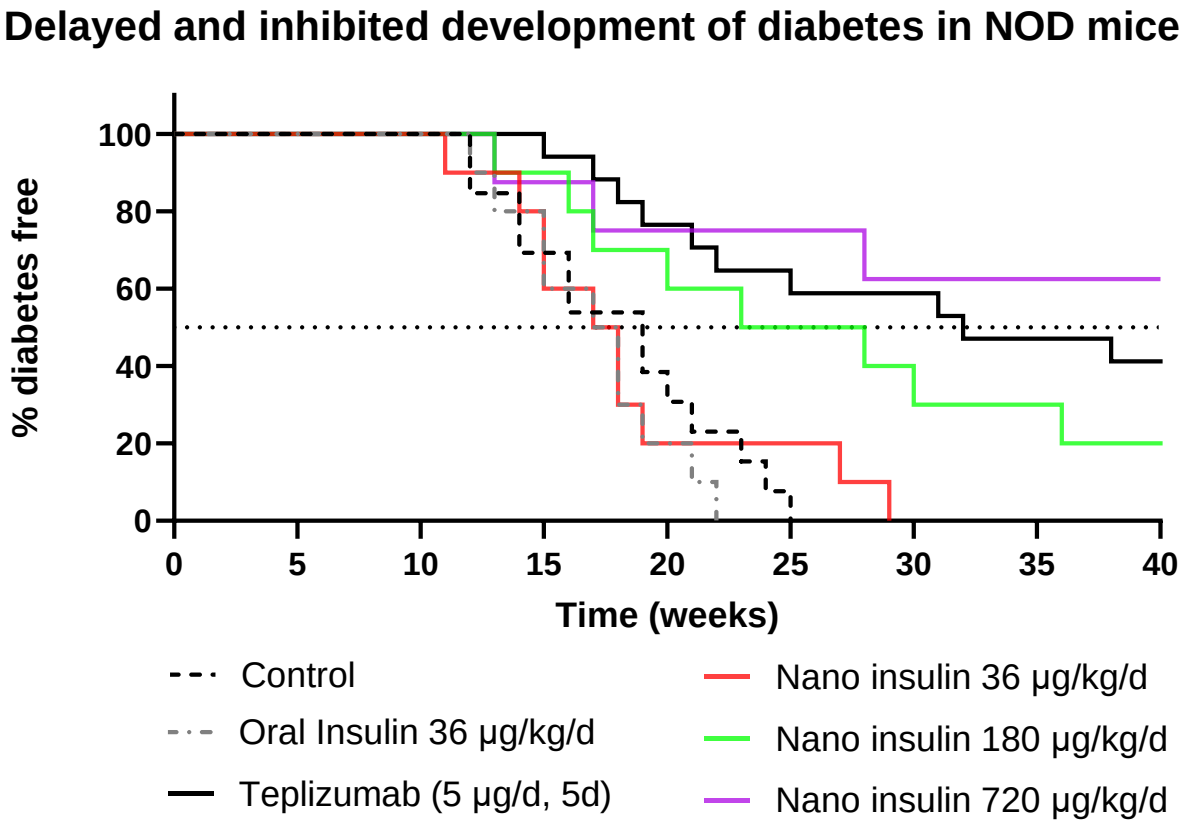


Kupffer cell



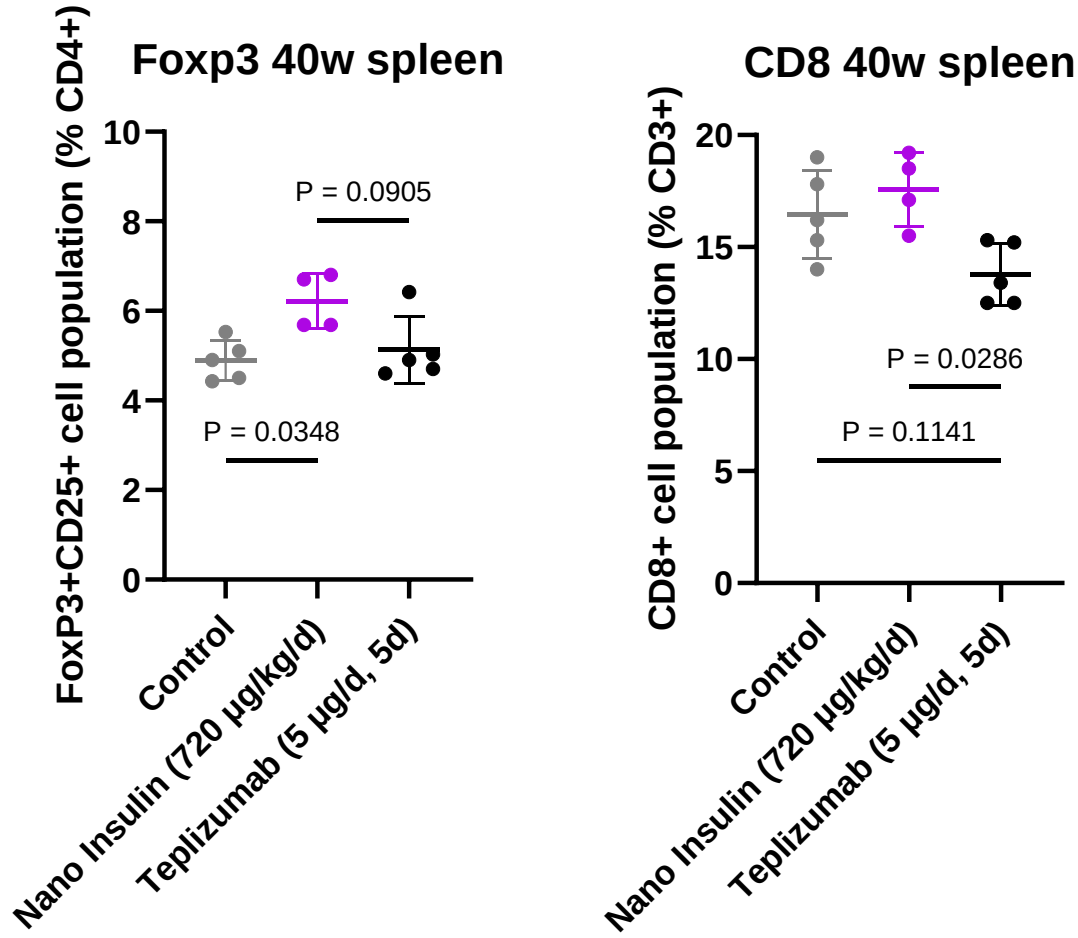
Treatment shows a dose dependent delay in diabetes in non-obese diabetic mice

- NOD mice
  - polygenic model for autoimmune T1D
- Nano insulin delays the onset of hyperglycaemia and outperforms Teplizumab
- Dose dependent effect of treatment



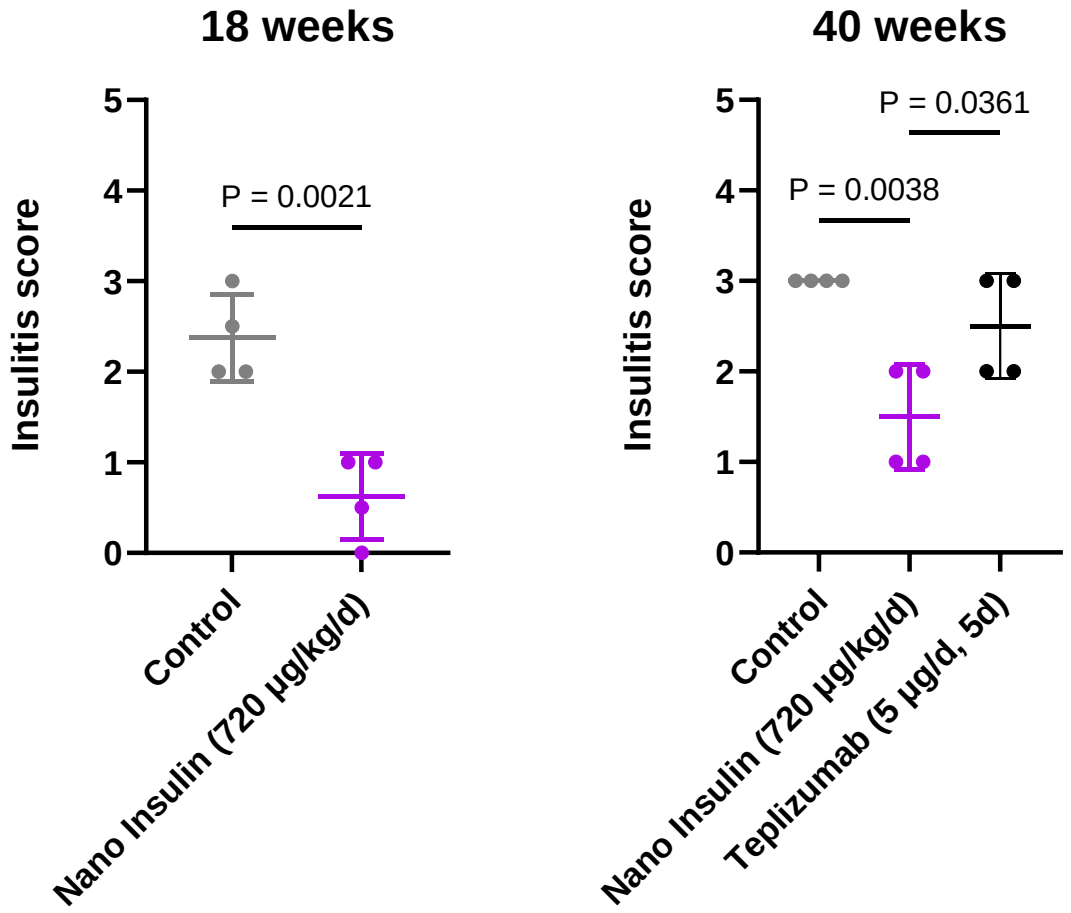
Splenocyte flow cytometry from 40w surviving NOD mice

- Nano insulin:
  - increased T reg cells
  - No change in CD8 cells
- Teplizumab
  - No change T reg cells
  - Decreased CD8 cells



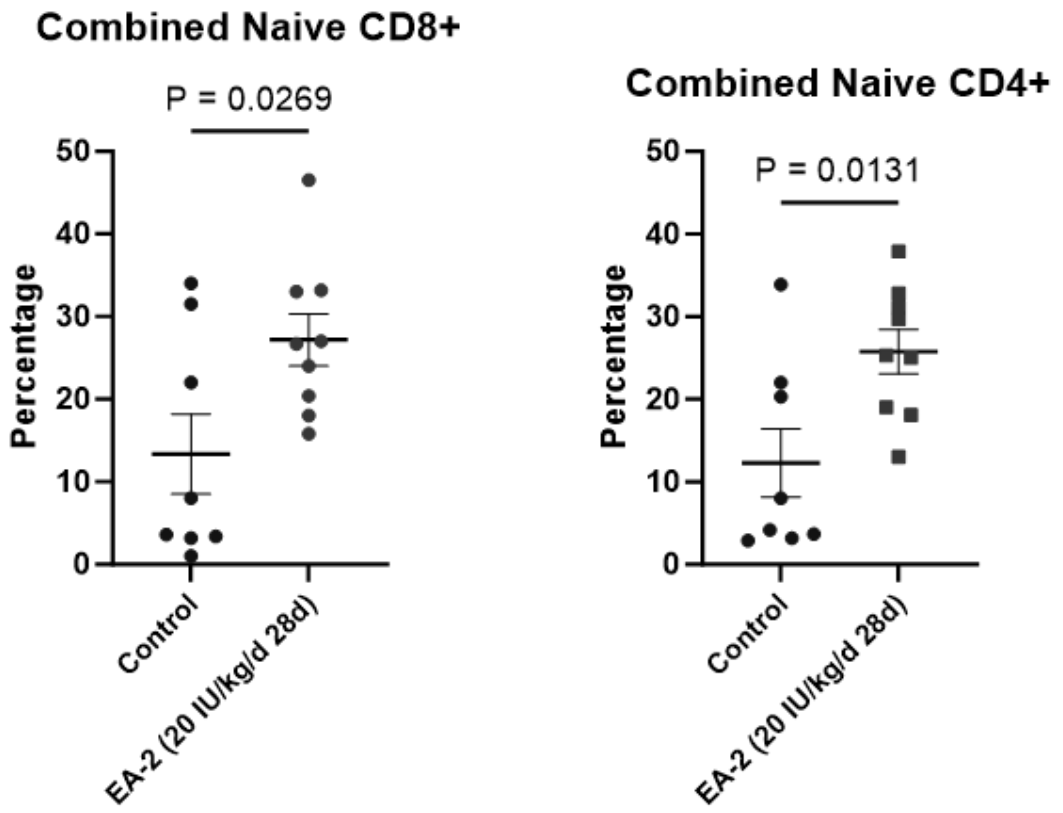
Reduced insulitis with nano insulin

- Nano insulin:
  - Reduction in insulitis at weeks 18 and 40.
  - Greater reduction compared to Teplizumab.



4w treatment induces T cell anergy in NOD mice

- Nano insulin:
  - Promotes anergy in both CD8 and CD4 T cells.
  - Effect is promoted with 28 days treatment.



Summary

- We have developed an:
  - an antigen transporting nano complex for selective delivery to antigen presenting cells.
    - We have shown this technology can include immune tolerance in T1D.
- The technologies are designed a plug and play system for proteins, antigens and gene modifying technology.

Team

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Australian Diabetes Society
NHMRC Emerging leaders
Medical Research Future Fund
Therapeutic Innovations Australia
Research Council of Norway
Haemophilia Foundation Australia

Commercial
Proto Axiom Pty Ltd
Endo Axiom Pty Ltd