IMMUNOLOGY OPPORTUNITY AT INSERM

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MUCOSAL VACCINATION TO INDUCE TOLERANCE & PREVENT AUTO-IMMUNE DISEASES (BIO15274)

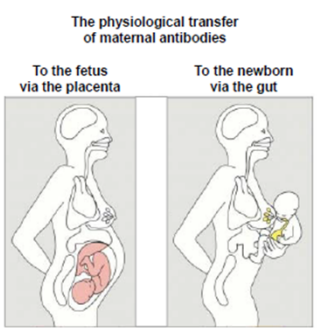
Product factsheet

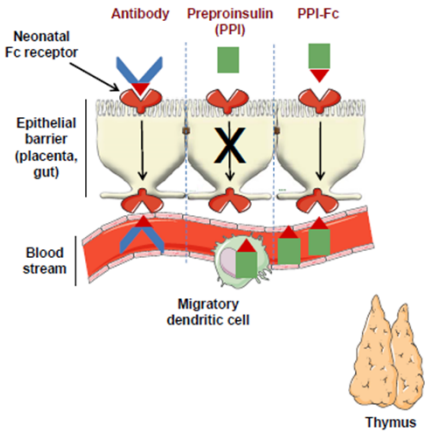
In vivo POC

- **Product candidate**: Fc-fused Ag, i.e. Preproinsulin (PPI) the T1D triggering antigen, thus allowing FcRn interaction and so epithelial barriers crossing

- **POC**:
  - PPI-Fc strategy which exploits the neonatal Fc receptor (FcRn) pathway that physiologically delivers maternal IgG to the offspring through the placenta during fetal life and through the gut during lactation were tested
  - PPI-Fc transplacental vaccination strategy was shown successfully in T1D mouse models

Vaccination strategies using Fc-coupled antigens





  - PPI-Fc orally administered to newborn mice is transferred across the gut and results in T-cell modifications suggestive of immune tolerance : as for transplacental delivery, only PPI-Fc reaches the circulation and is ferried to the thymus mice, resulting in decreased numbers of CD8+ Teffs and increased numbers of CD304+FoxP3+CD4+ Tregs.

- **Publications** : Materno-fetal transfer of preproinsulin through the neonatal Fc receptor prevents autoimmune diabetes Culina S. et al. Diabetes. 2015 Oct;64(10):3532-42.

- **Patent applications**:
  - WO/2017/012959 : METHODS AND PHARMACEUTICAL COMPOSITIONS FOR INDUCING IMMUNE TOLERANCE BY MUCOSAL VACCINATION WITH FC-COUPLED ANTIGENS.
  - US15/190,272 : PRENATAL THERAPY TO INDUCE IMMUNE TOLERANCE

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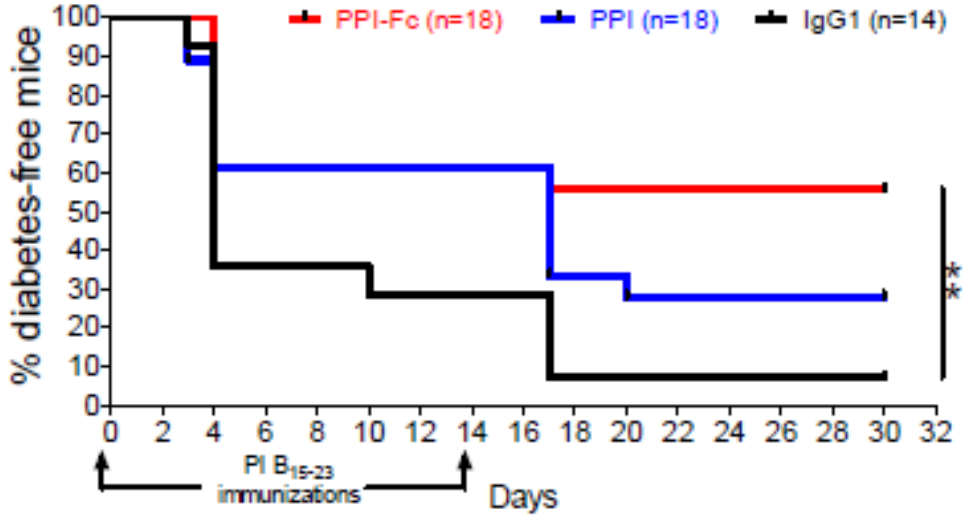
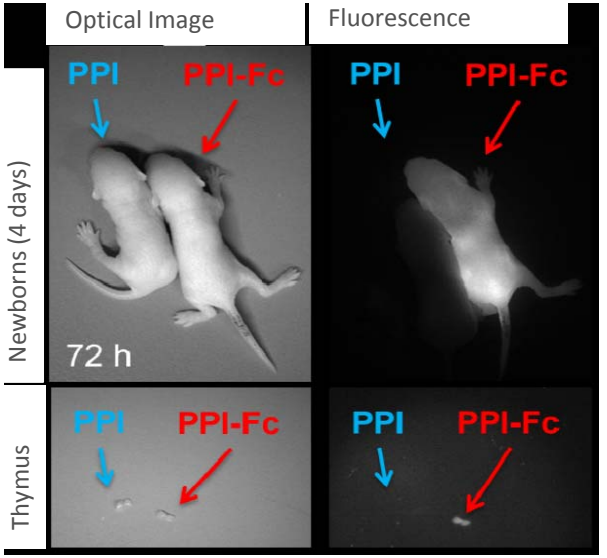
Proof of concept

- Oral vaccination strategy with Fc-coupled β-cell antigens for type I diabetes treatment, in rodent model

PPI-Fc gut transfer reduces diabetes incidence



A. Diabetes incidence following PPI_{B15-23} prime-boost immunization in the offspring of G9C8 NOD mice.



B. 4-day-old G9C8 newborns were force-fed with Alexa-labeled PPI-Fc or PPI (50 µg) and their whole bodies and thymi imaged after 72 h.

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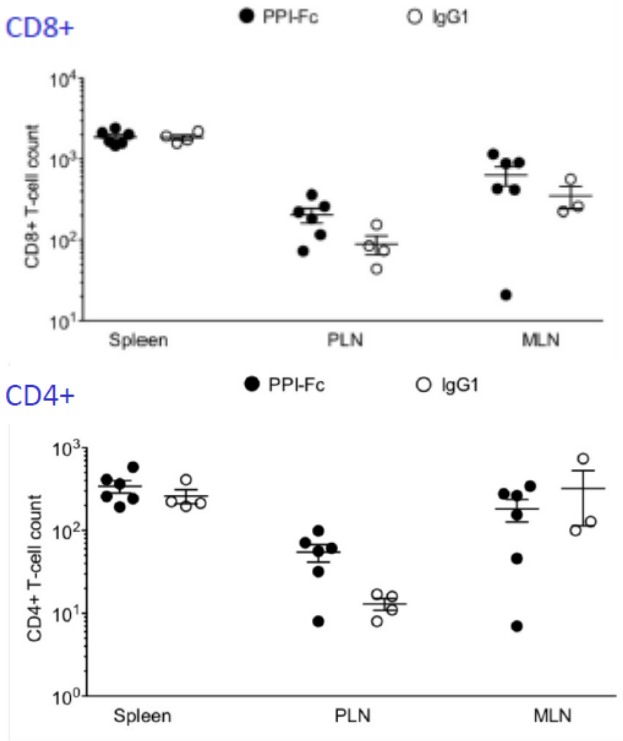
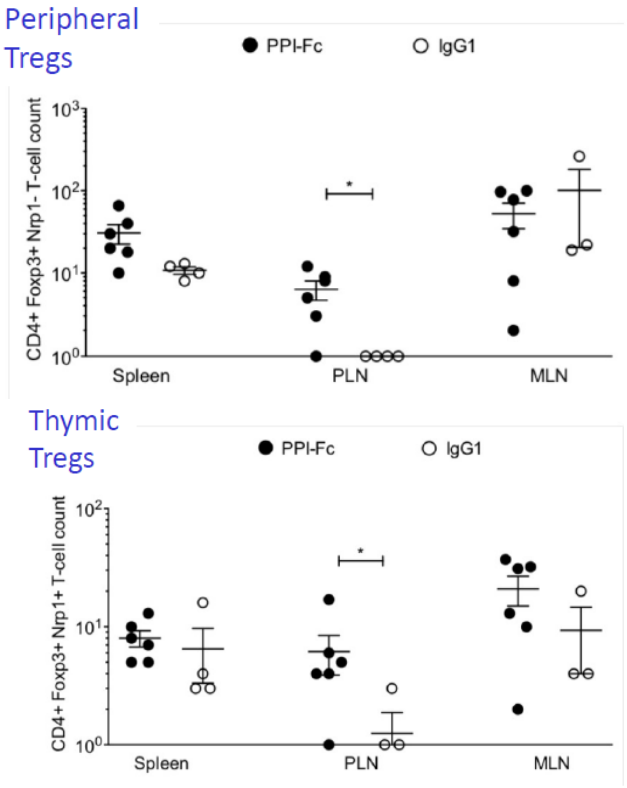
Proof of concept

- Oral vaccination strategy with Fc-coupled β-cell antigens for type I diabetes treatment, in rodent model

PPI-Fc orally administered directly to newborn mice induces T-cell modifications suggestive of tolerance induction



A. Percent of $CD8^+CD3^+$ and $CD4^+CD3^+$ T cells in 4-week-old G9C8 mice treated at 1-day of life



B. Percent $CD4^+$ T-cell subsets in the same mice.

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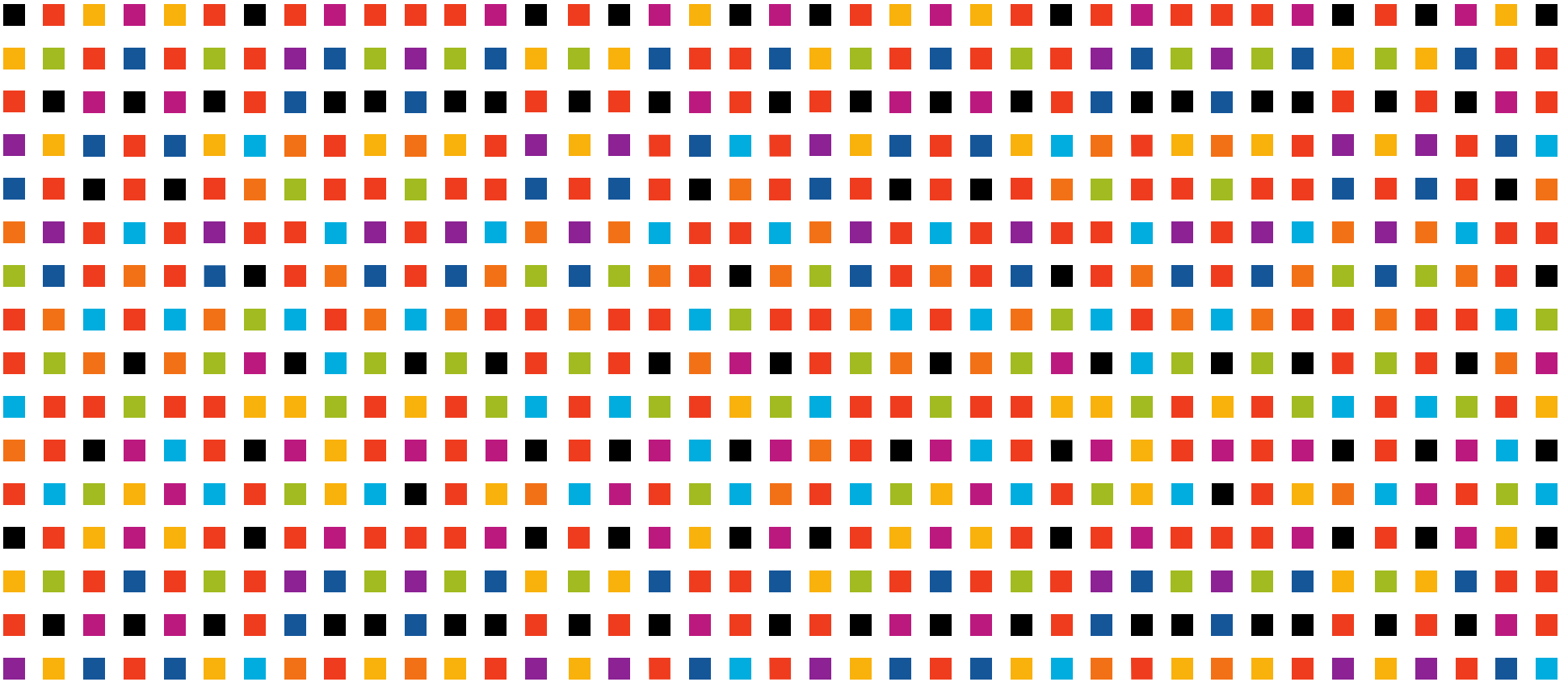

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