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Biological Sex Modulates The Effects of The Immunoregulatory Fibrinogen-like Protein 2 Molecule on Alloimmunity

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The Presenter Has no Financial Conflict to Disclose

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Biological Sex Modulates The Effects of The Immunoregulatory Fibrinogen-like Protein 2 Molecule on Alloimmunity

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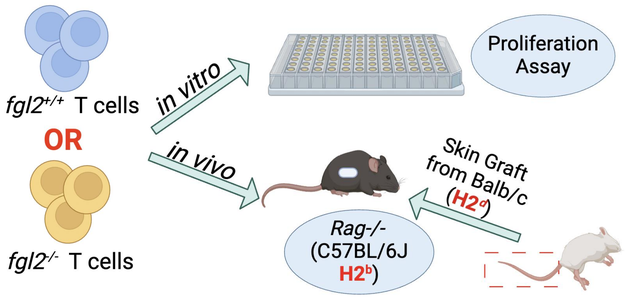
1 Introduction

- The effects of sex differences on patients' outcome post-transplant remain poorly understood and understudied.
- We know that females tend to mount more robust immune responses compared to males due to estrogen in the former and androgen in the latter.
- The immunoregulatory **fibrinogen-like protein 2 (fgl2)** molecule, holds potential as tolerizing therapy.

Hypothesis

Fgl2's effect on the allograft response is sex dependent.

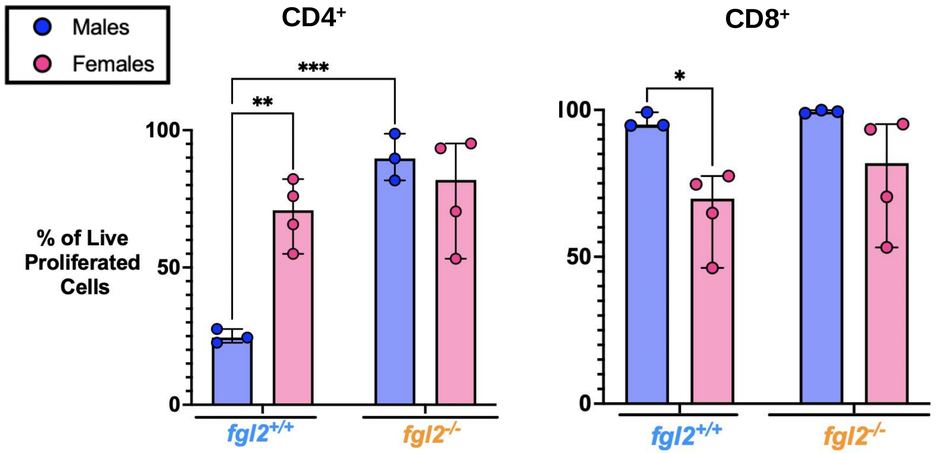
2 Method



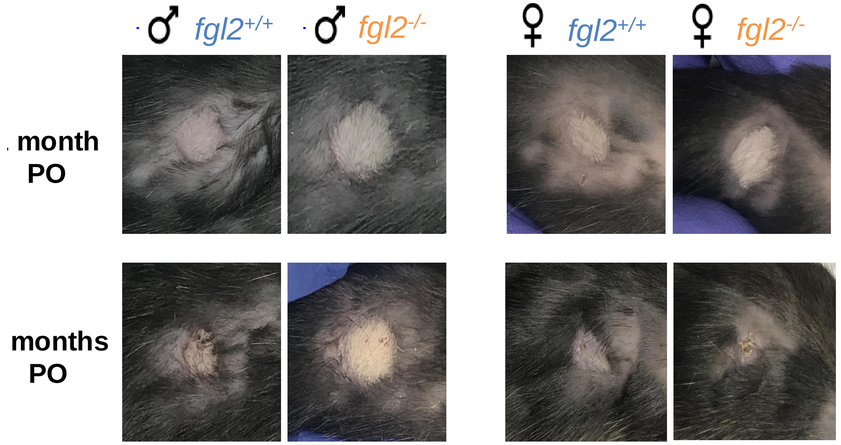
- ***in vitro***: T cell isolation & activation
- ***in vivo***: Adoptive T cell transfer into *Rag*$^{-/-}$ recipients (T cell-deficient), followed by a skin graft from Balb/c donor
- Both cells and graft donors were matched to the recipients' sex

3 Results

Fgl2 influences *in vitro* proliferation of T cells in a sex-dependent manner



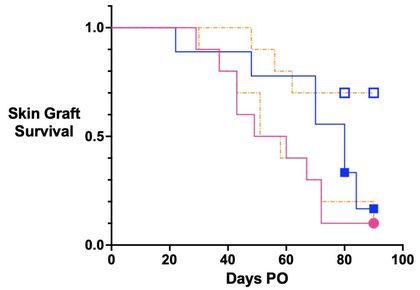
Proliferation of male and female CD4$^+$ (**p= 0.014, ***p= 0.001) and CD8$^+$ (*p=0.0145) T cells from either *fgl2*$^{+/+}$ or *fgl2*$^{-/-}$ mice . Statistics obtained from 2way ANOVA.



Skin graft on *Rag*$^{-/-}$ recipients of *fgl2*$^{+/+}$ and *fgl2*$^{-/-}$ T cells at approx. 1 month and 2 months PO.

4 Results

Biological sex influences Fgl2's regulation on the rejection kinetics of skin grafts



	n	MST (days)
♀ *fgl2*$^{+/+}$ *T cells*	9	54.5
♀ *fgl2*$^{-/-}$ *T cells*	9	54.5
♂ *fgl2*$^{+/+}$ *T cells*	7	80
♂ *fgl2*$^{-/-}$ *T cells*	3	undefined

Survival curves of all four groups. P-value based on Log-rank Mantel-Cox test. **MST** = median survival time.

5 Conclusions

- Intrinsic expression of Fgl2 in T cells downregulates the proliferation of CD4$^+$ cells *in vitro*; this effect is not observed in female T cells
- Although *in vivo* data showed that fgl2 expression from T cells did not affect graft rejection, female T cells rejected *Balb/c* grafts faster than male T cells.
- This suggests that T cell extrinsic fgl2 in the *Rag*$^{-/-}$ environment may have contributed to slowing graft rejection mediated by male T cells.