



CHANGE THE WORLD FROM HERE



Torn between two diseases: Alteration in TGF β Signaling Prevents Diabetes but Promotes Neuropathy

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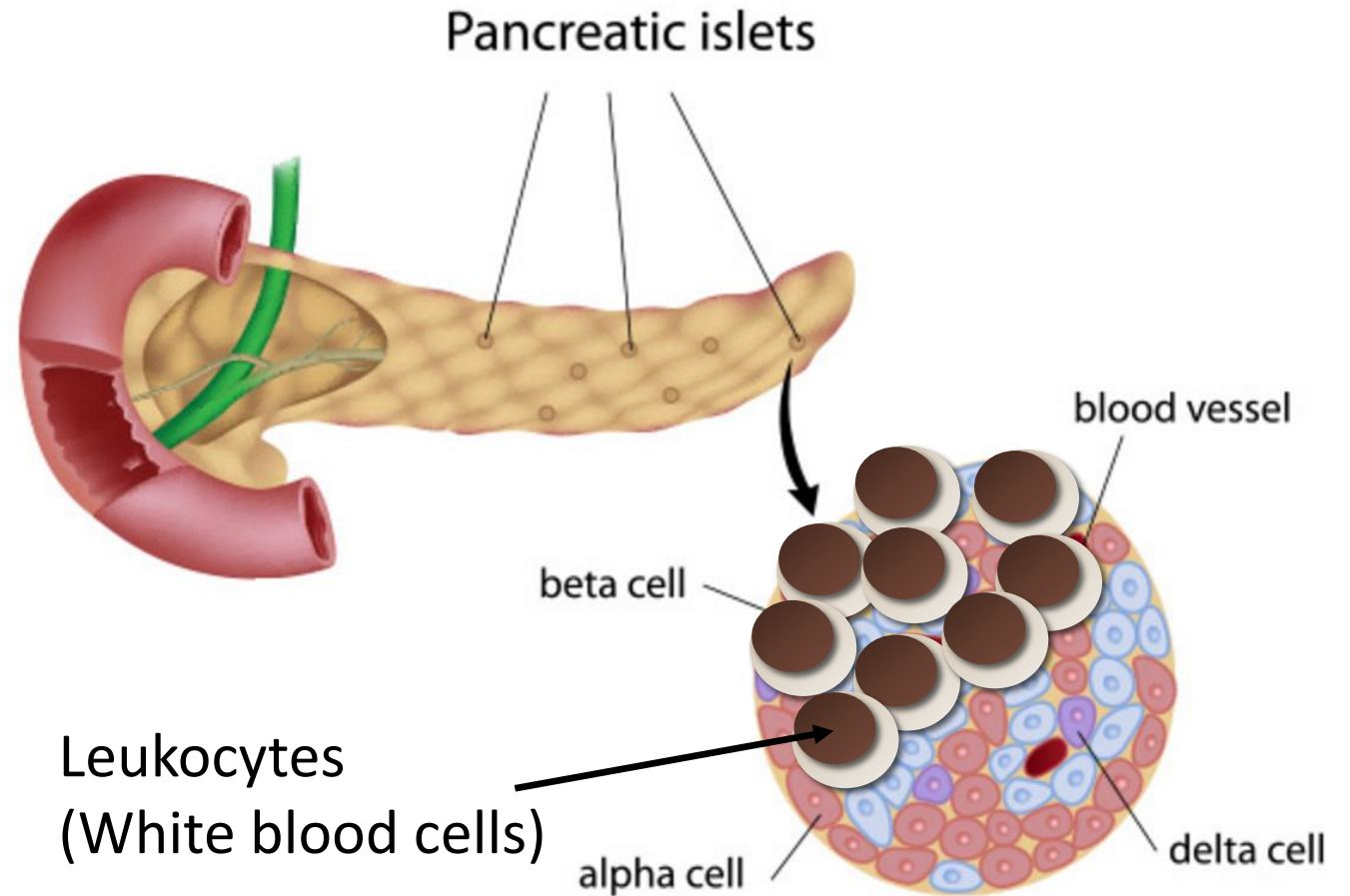
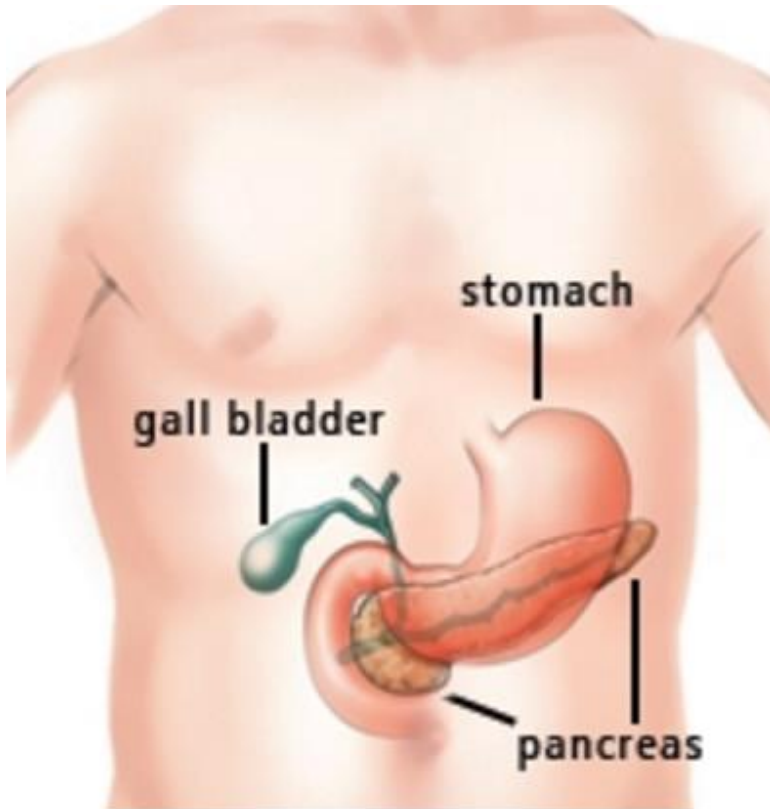
BIOLOGY MAJOR & NEUROSCIENCE, CHEMISTRY MINORS

CREATIVE ACTIVITY & RESEARCH DAY, APRIL 22ND 2016

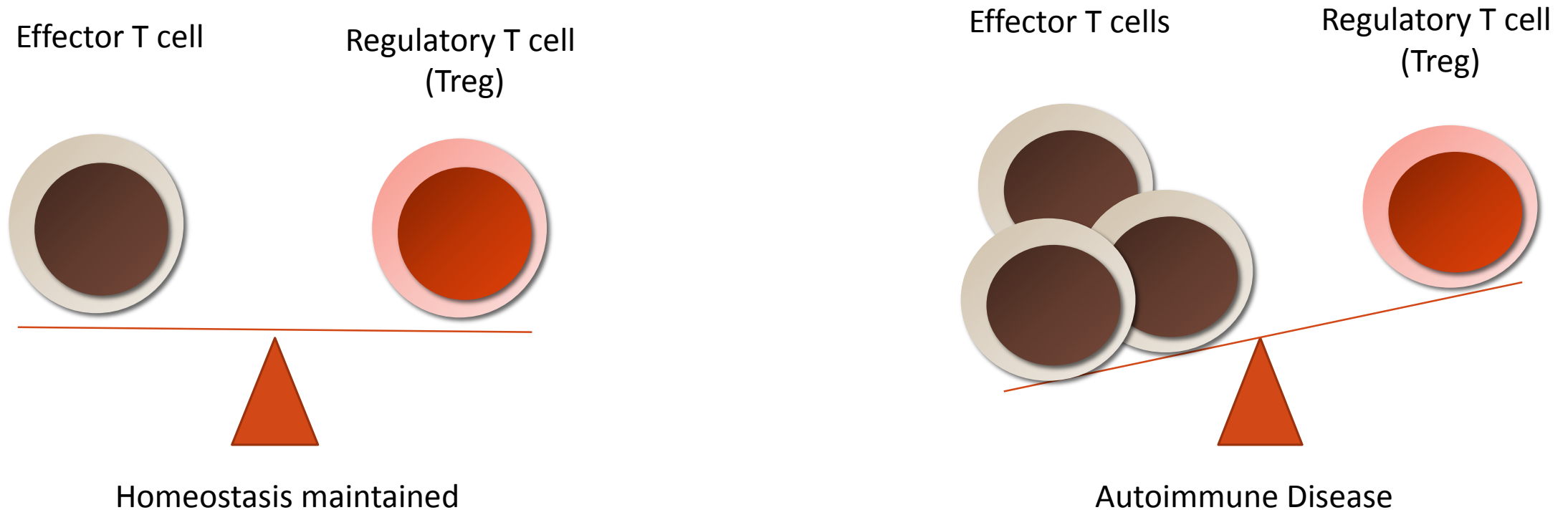
What is Type 1 (Juvenile-Onset) Diabetes?

- ❖ Autoimmune disease where the pancreatic beta cells are destroyed by autoreactive T and B cells
 - ❖ Results in lack of insulin production and high glucose in blood
- ❖ Patients must take exogenous insulin for the remainder of their lives
- ❖ Associated with severe complications: cardiovascular, kidney, nerve damage
- ❖ Generally considered a disease of childhood
 - ❖ Approximately 3 million Americans have type 1 diabetes
 - ❖ Prevalence is increasing every year

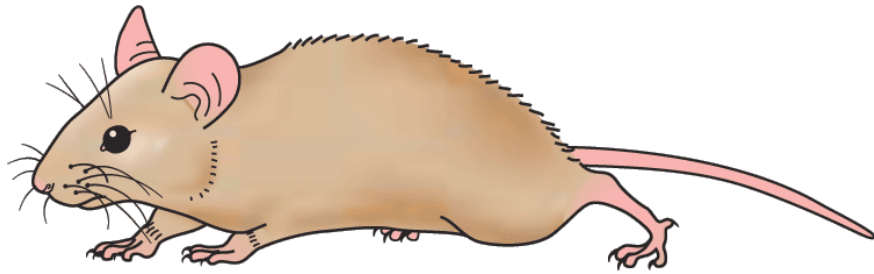
Lymphocytes destroy pancreatic islets in T1D



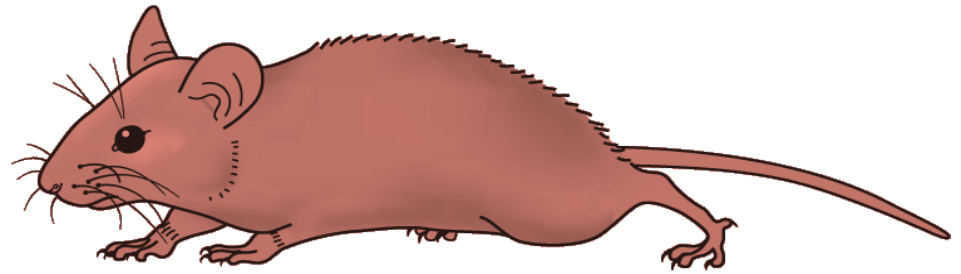
Dysregulation between regulatory and effector mechanisms precipitates autoimmunity



The non-obese diabetic (NOD) mouse models human type 1 diabetes



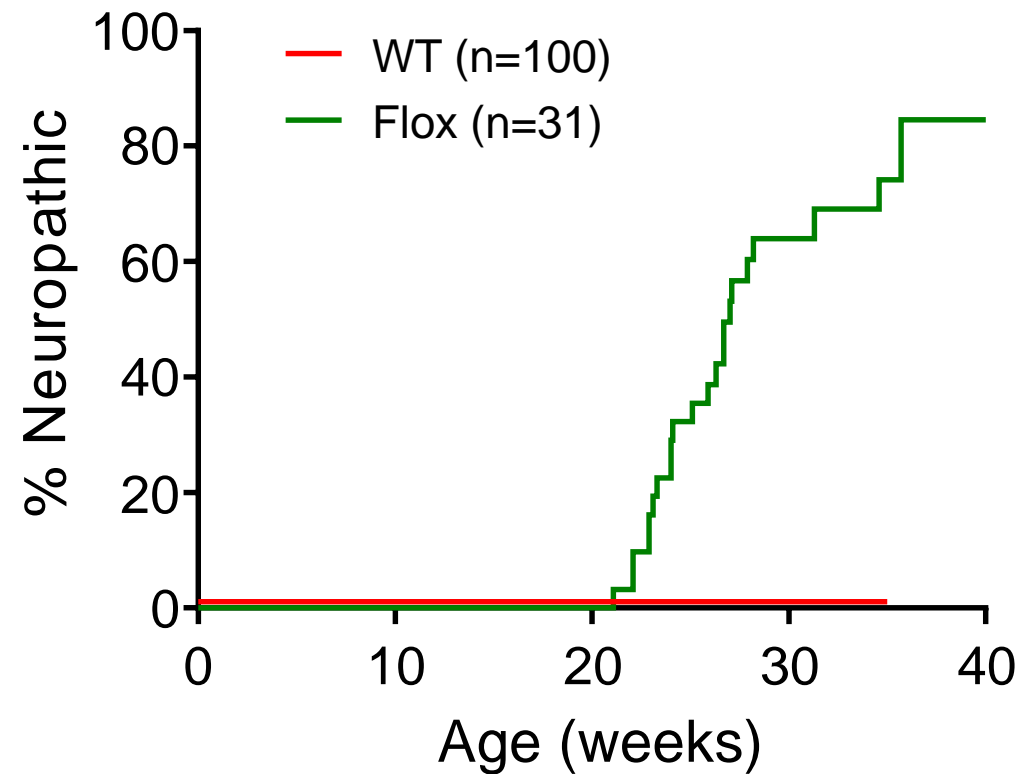
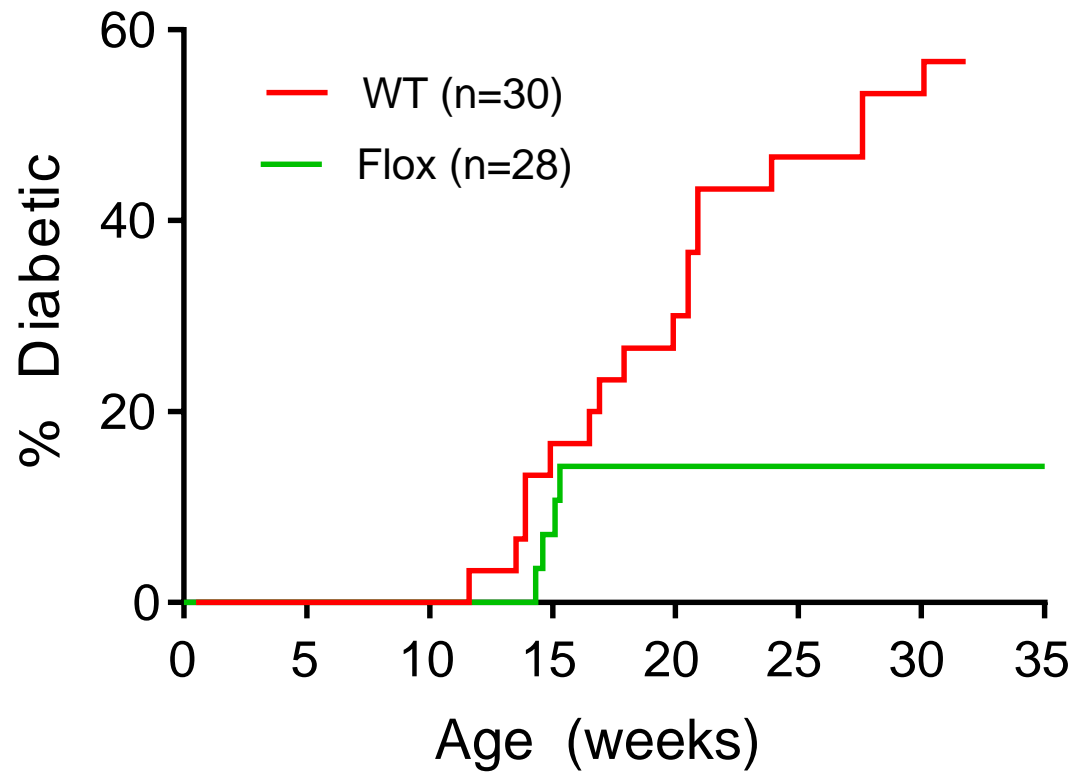
NOD mouse
“Wild type (WT)”



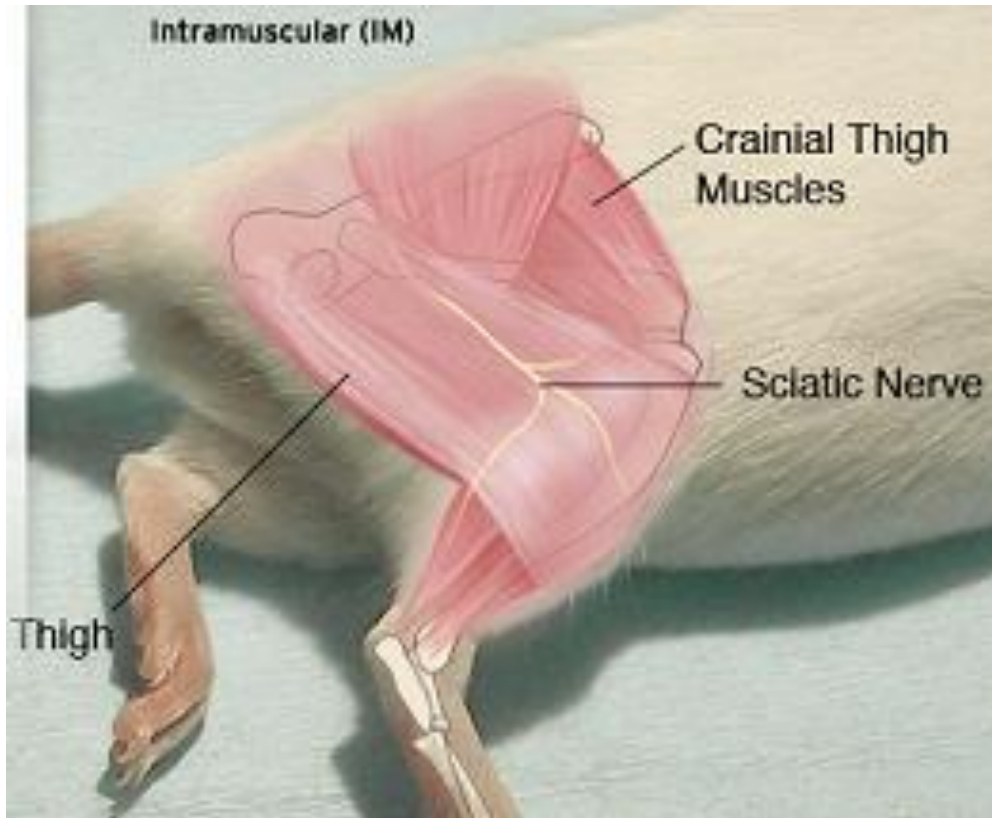
Foxp3-Cre x TGFbRII Δ/Δ
“Flox”

Cell type specific deletion of TGF β receptor
MEANS – there is no TGF β signaling in
regulatory T cells

WT and Flox mice seem to develop opposing either diabetes OR neuropathy



What is neuropathy?

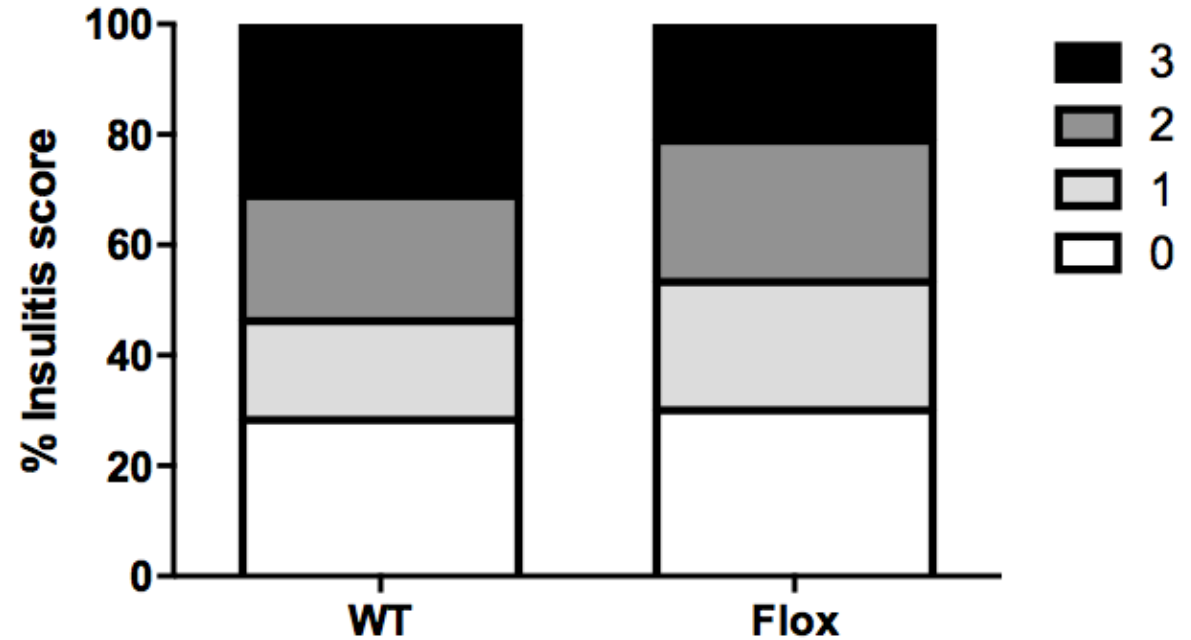
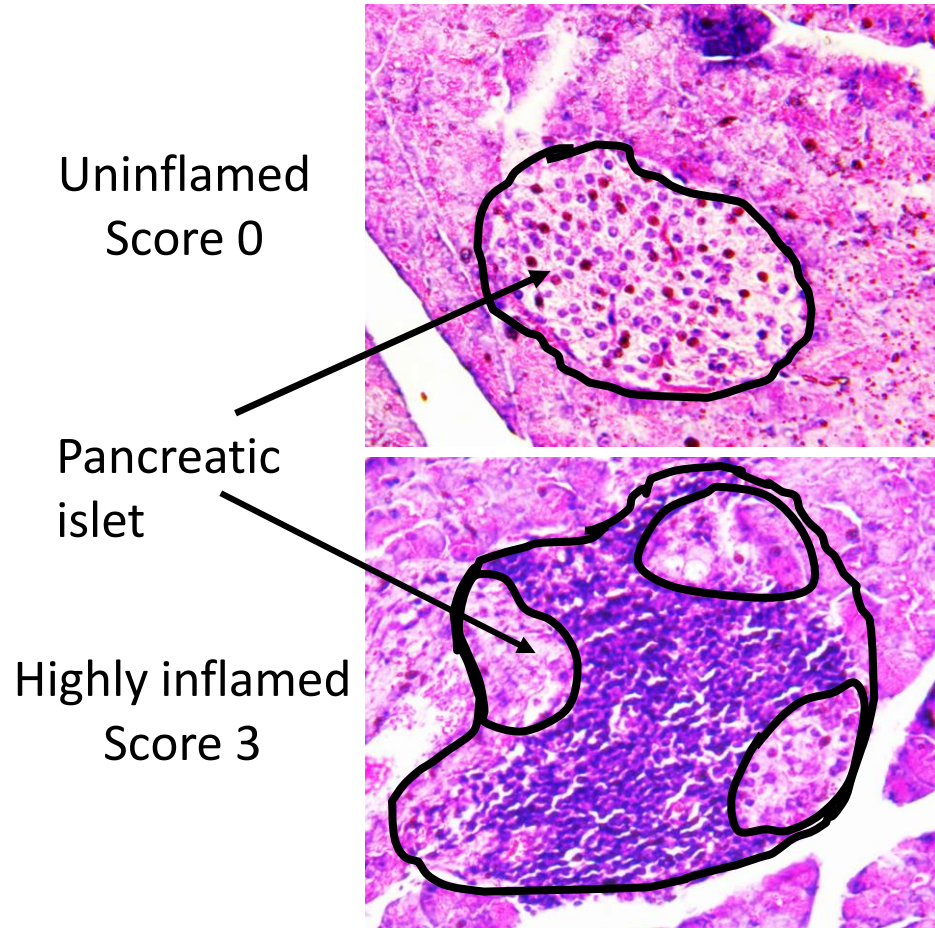


Does the loss of TGF β signaling in Tregs
affect or lead to inflammation in
different tissues?

Pancreas
Sciatic Nerve
Salivary gland
Thyroid
Heart

Ovary
Kidney
Small intestine
Liver
Lung

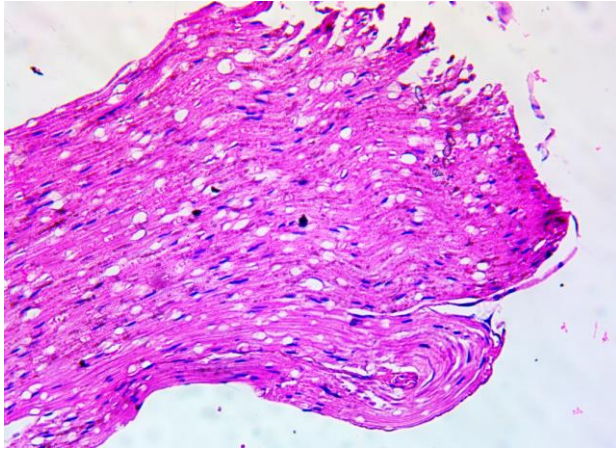
Inflammation observed in Flox islets similarly to WT NOD islets



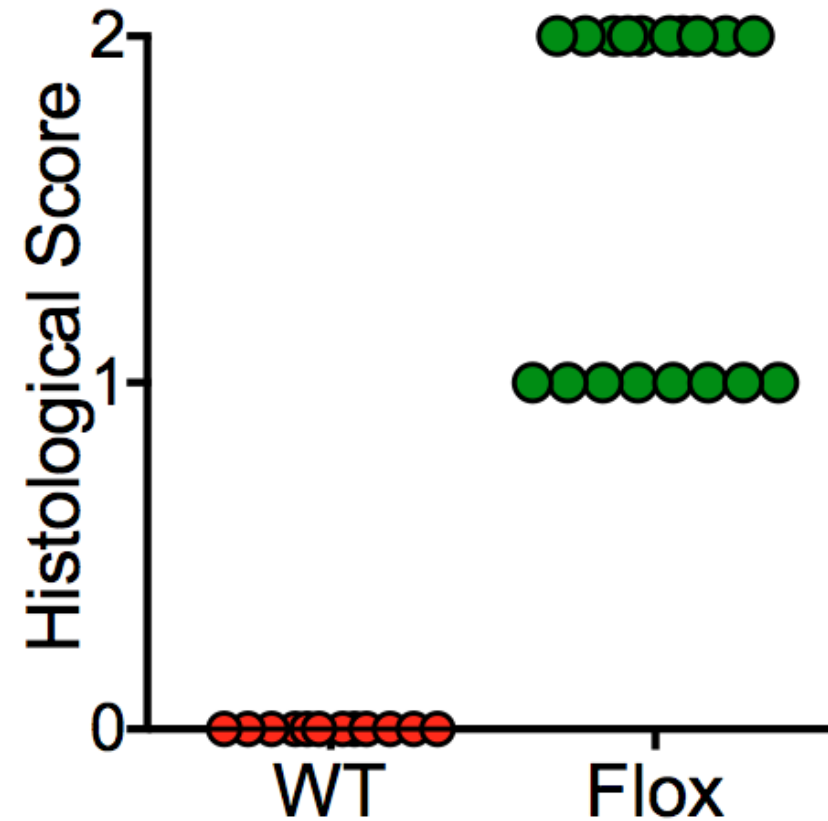
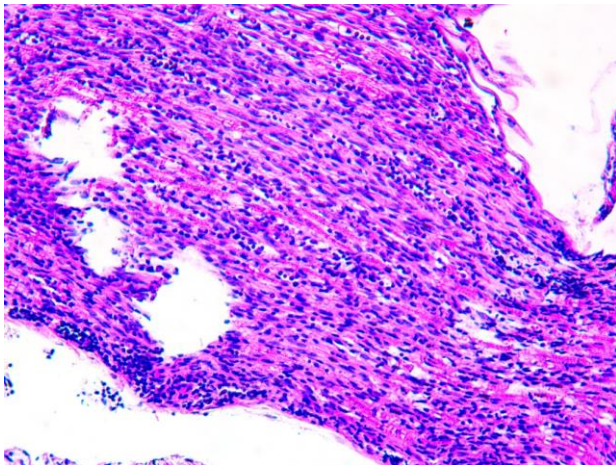
Dark purple spots - leukocytes

Is neuropathy associated with inflammation in the sciatic nerve?

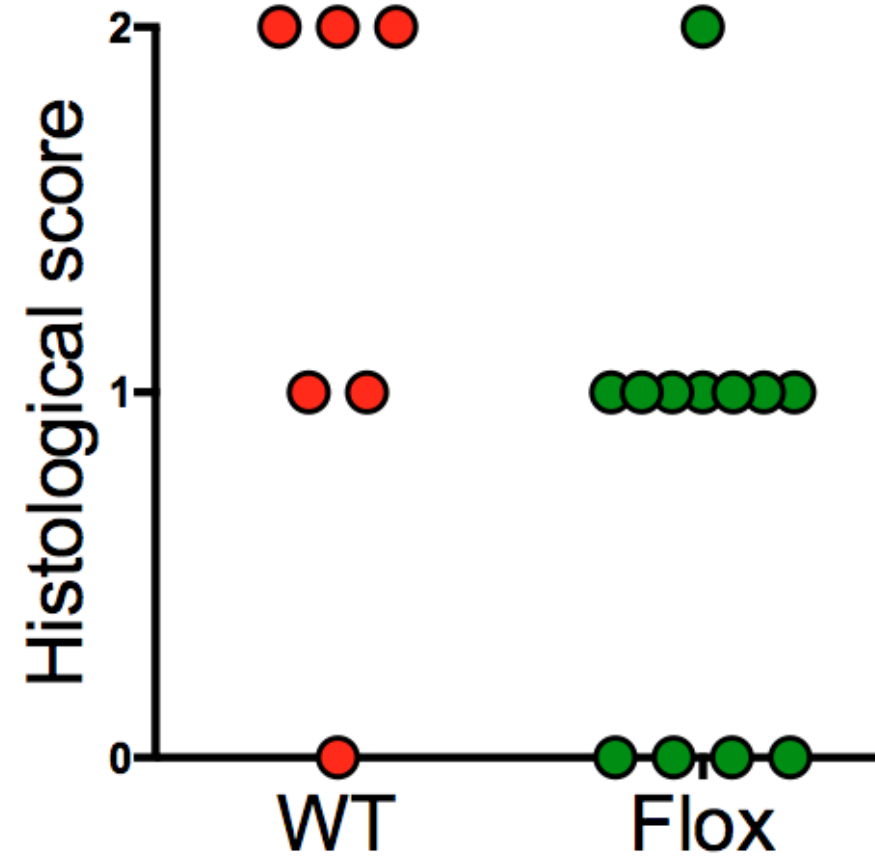
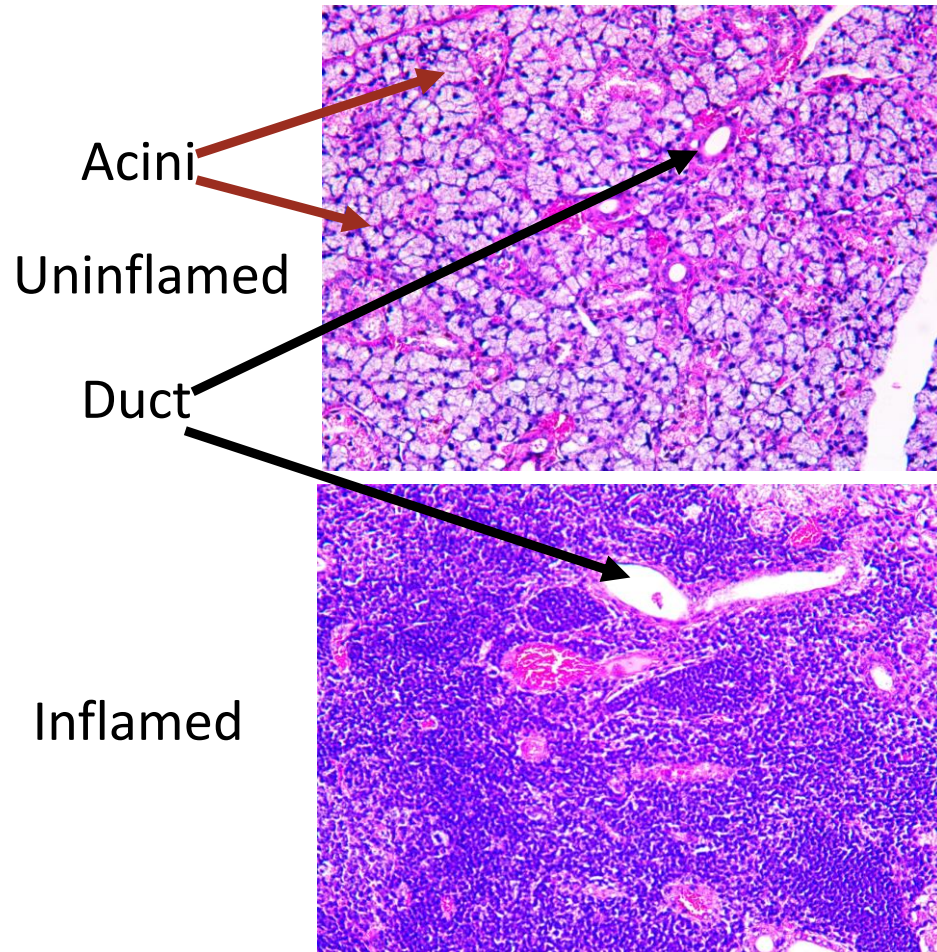
WT -
uninflamed



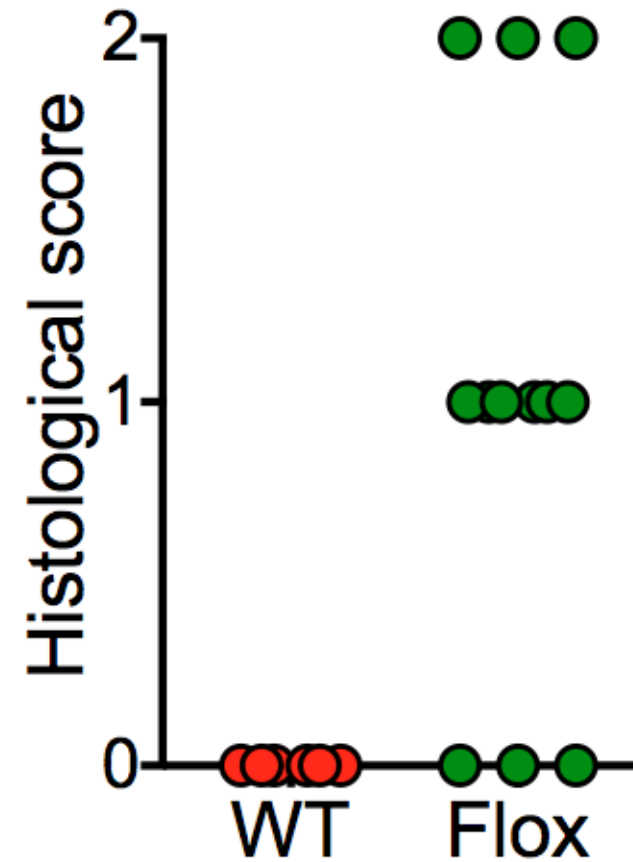
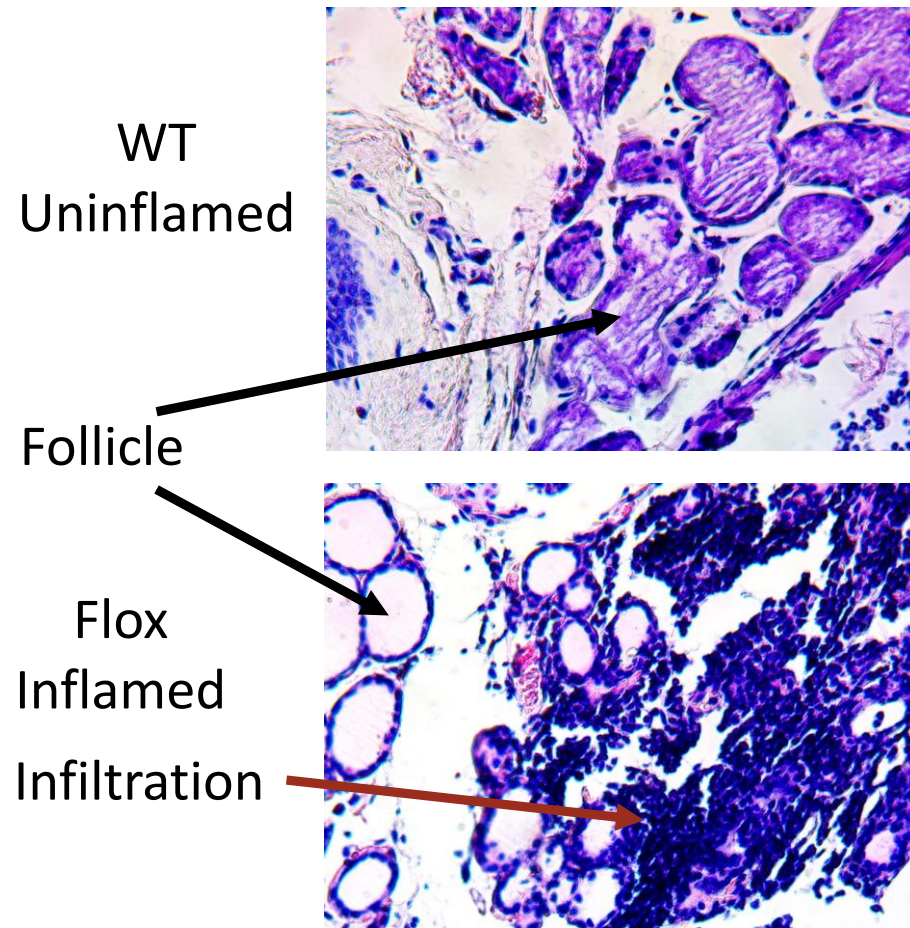
Flox – heavily
inflamed
(score 2)




Less inflammation in Flox submandibular gland than WT NOD mice



Novel thyroid inflammation in Flox mice compared to WT NOD mice



Conclusions: Loss of TGF β signaling in Tregs leads to inflammation in different tissues

Organ	WT	Flox
Pancreatic Islets	+ ( Db)	+ ( Db)
Sciatic Nerve	-	++
Submandibular Gland	++	+
Thyroid	-	+

Future Directions

❖ Short term:

- ❖ Finish analyzing the rest of the organs – any other autoimmune diseases present in these mice
- ❖ Analyze more WT NOD mice for confirmation of the phenotypes

❖ Long term:

- ❖ Describe the mechanism of disease development in these different NOD mouse models

Acknowledgements

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Thank you all for listening!



Questions?
