

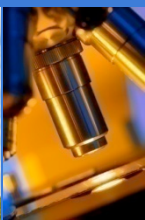
Aire expression in human spleen & lymph nodes: a comparison of type-1 diabetics & healthy controls

Eileen McMahon

In collaboration with Todd Metzger

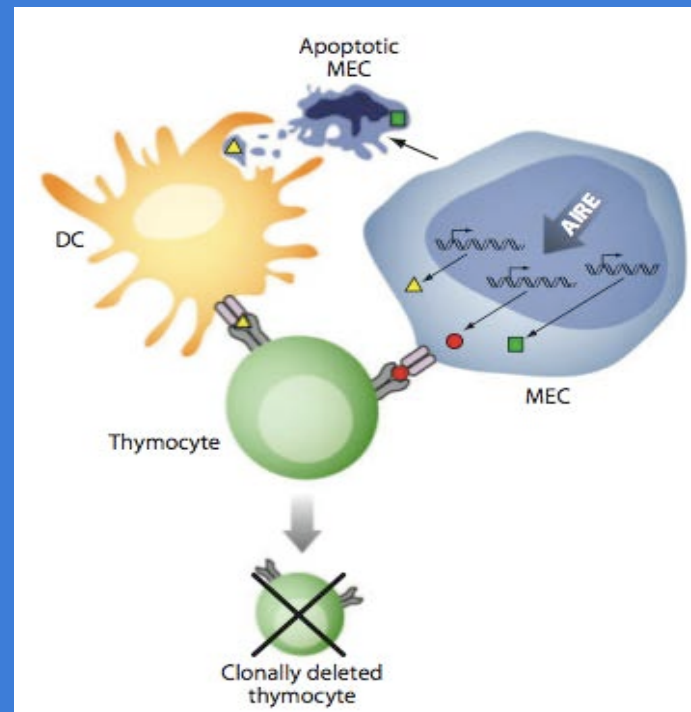
Anderson Lab

nPOD Annual Meeting – Jan., 2012

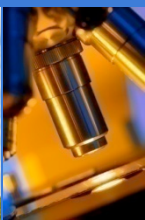


Autoimmune Regulator (Aire)

- First described in 1997 as cause of APS-1
- Transcription factor expressed in thymic epithelial cells (mTECs)
- Induces expression of tissue-specific antigens (TSAs) for neg. selection

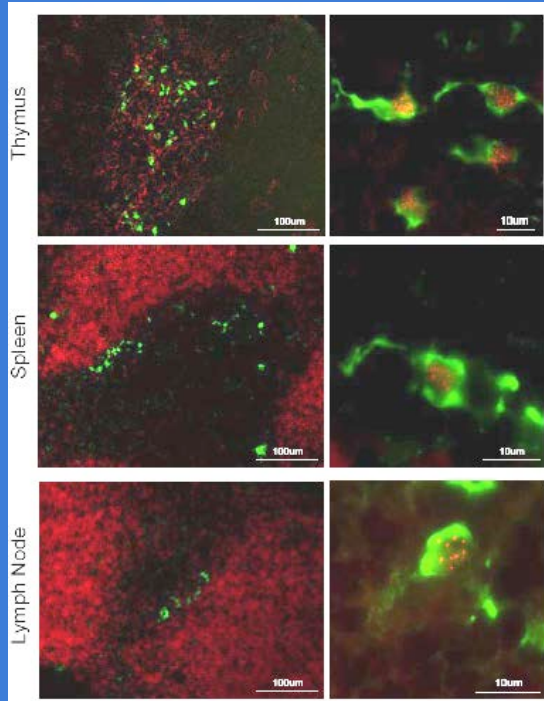


Mathis & Benoist, 2009

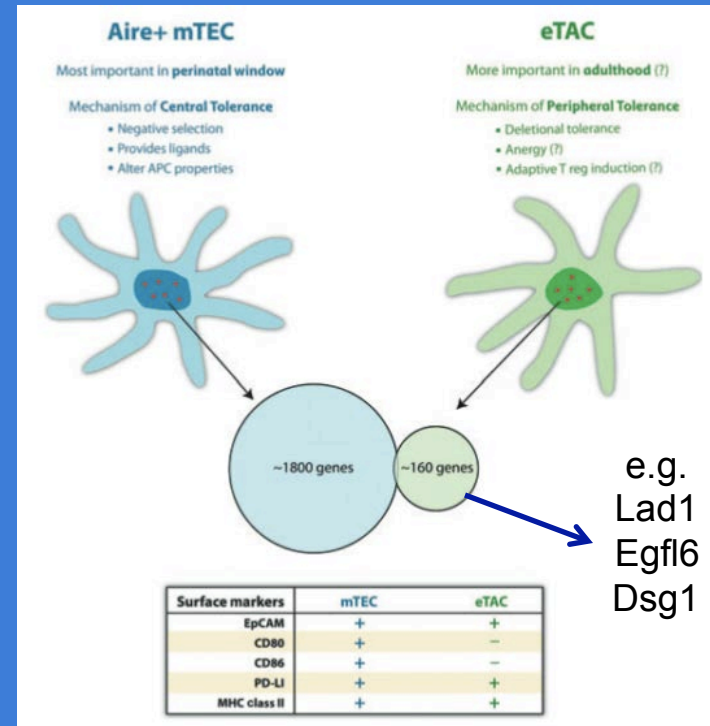


Extra-thymic Aire-expressing cells (eTACs)

Mouse

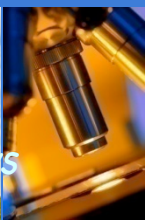


B220 **Aire**
Aire-driven GFP



nPOD

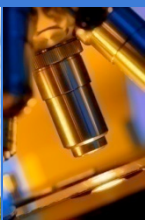
Network for Pancreatic Islet Transplantation
 Donors with Diabetes



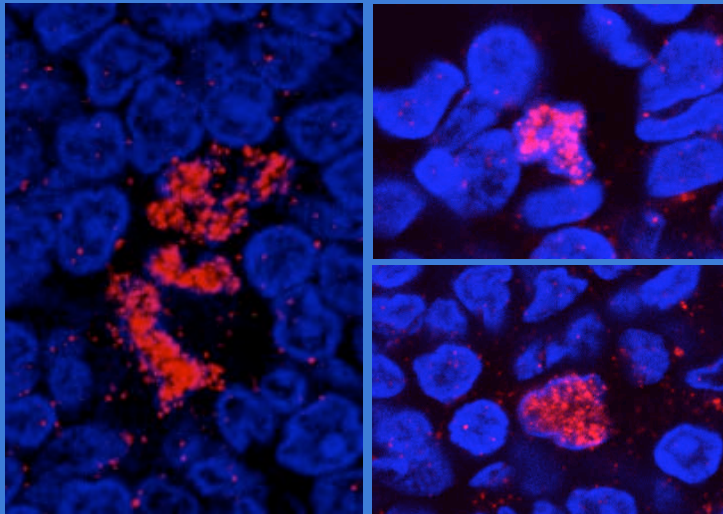
Metzger & Anderson, 2010 Imm. Reviews

Experimental questions & strategies

- Can eTACs be found in human LNs & spleen; if so, what do they express?
 - ✧ By immuno-fluorescence (PLN and non-PLN sections)
- Comparison of expression in T1D & non-T1D pancreatic LNs (quantitative RT-PCR)
 - ✧ Do they differ in Aire expression?
 - ✧ Does Aire expression correlate with expression levels of putative peripheral TSAs?



Aire⁺ cells found in pancreatic & non-pancreatic human lymph node

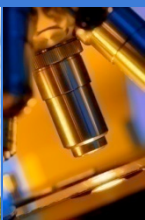


*6/6 non-T1D cases
examined:*

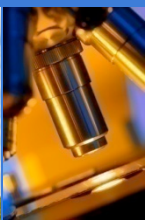
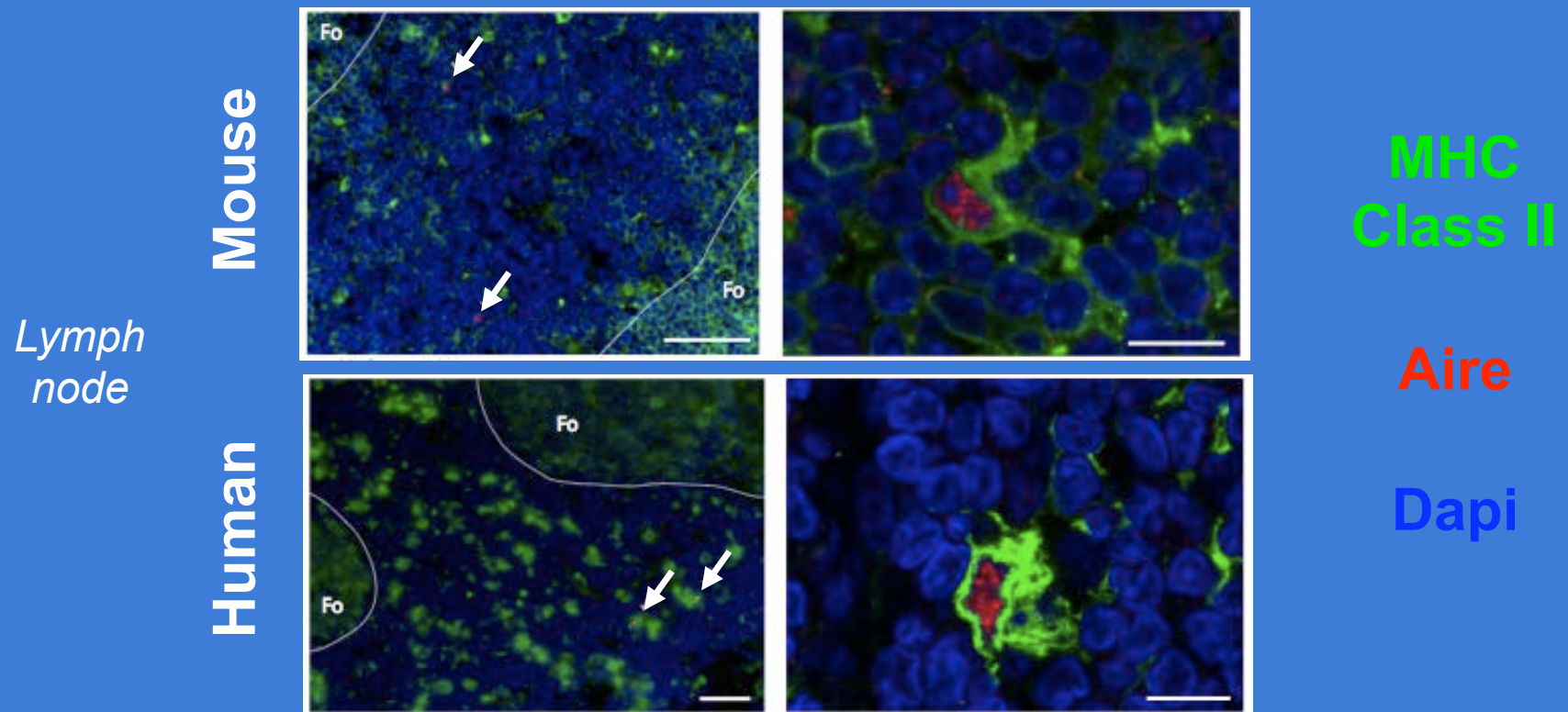
*5 PLN (6075, 6011,
6098, 6024, 6102)*

*4 nPLN (6020, 6011,
6098, 6024)*

Aire **Dapi**



Human eTACs mirror mouse eTACS in expression and location

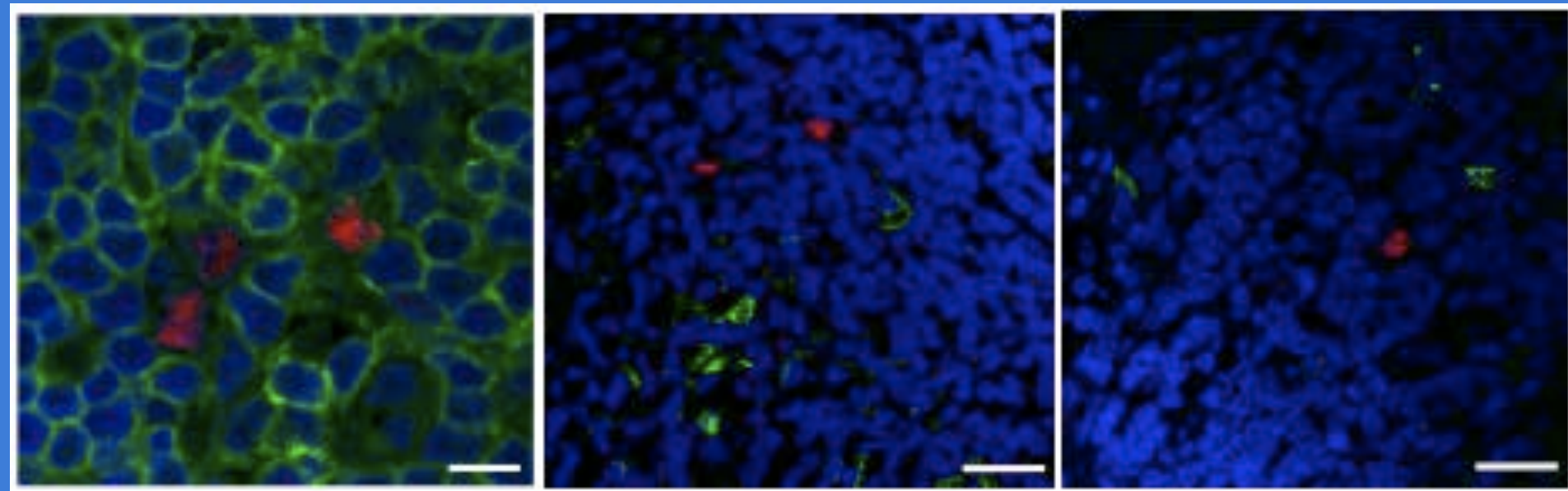


Similar to mouse, human eTACs are CD45^{lo}
and lack expression of CD11c & CD11b

CD45

CD11c

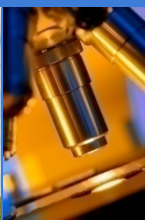
CD11b



Dapi Aire

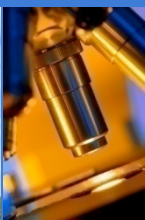


nPOD
Network for Pancreatic Organ
Donors with Diabetes



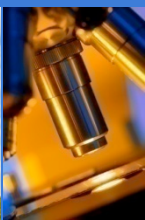
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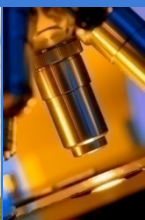
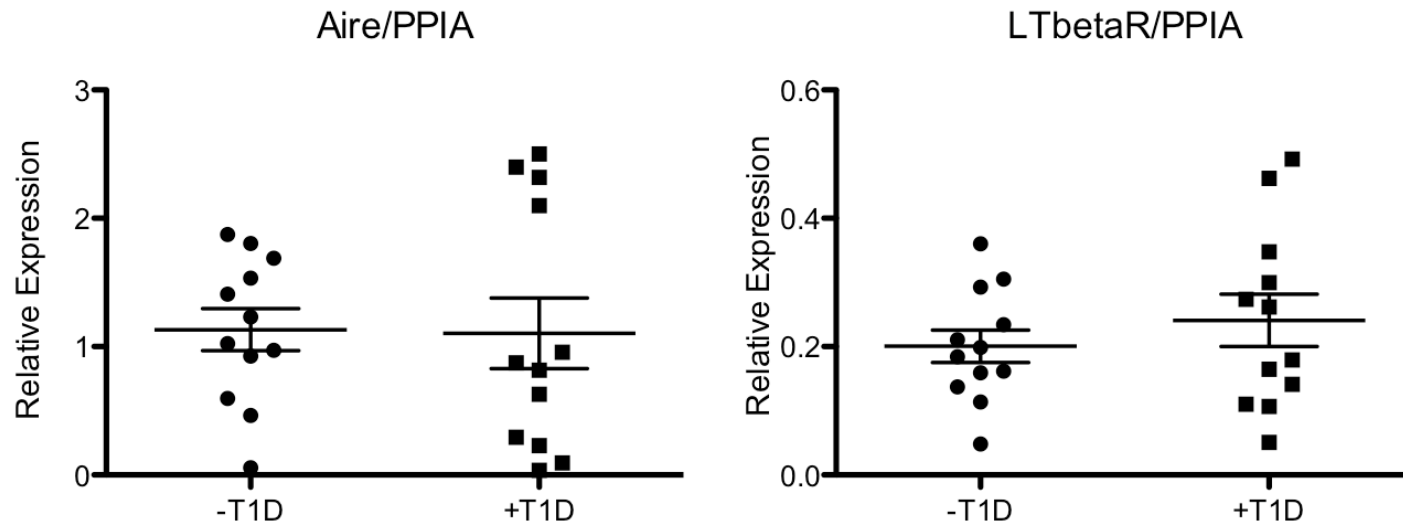


Summary information for sample groups

	No Diabetes	Type 1 Diabetes
<i>N numbers</i>		
Total	12	12
M	7	7
F	5	5
<i>Age</i>		
range	3-45	4-50
mean	26.4	25.6
<i>Ethnicity</i>		
Af. American	2	2
Caucasian	8	9
Hispanic	1	1
Unspecified	1	-
Average BMI (+/-SD)	27.6 +/- 6.9	25.1 +/- 4.0
<i>AutoAb status</i>		
no serum/not tested	1	2
negative	11	3
positive	0	7

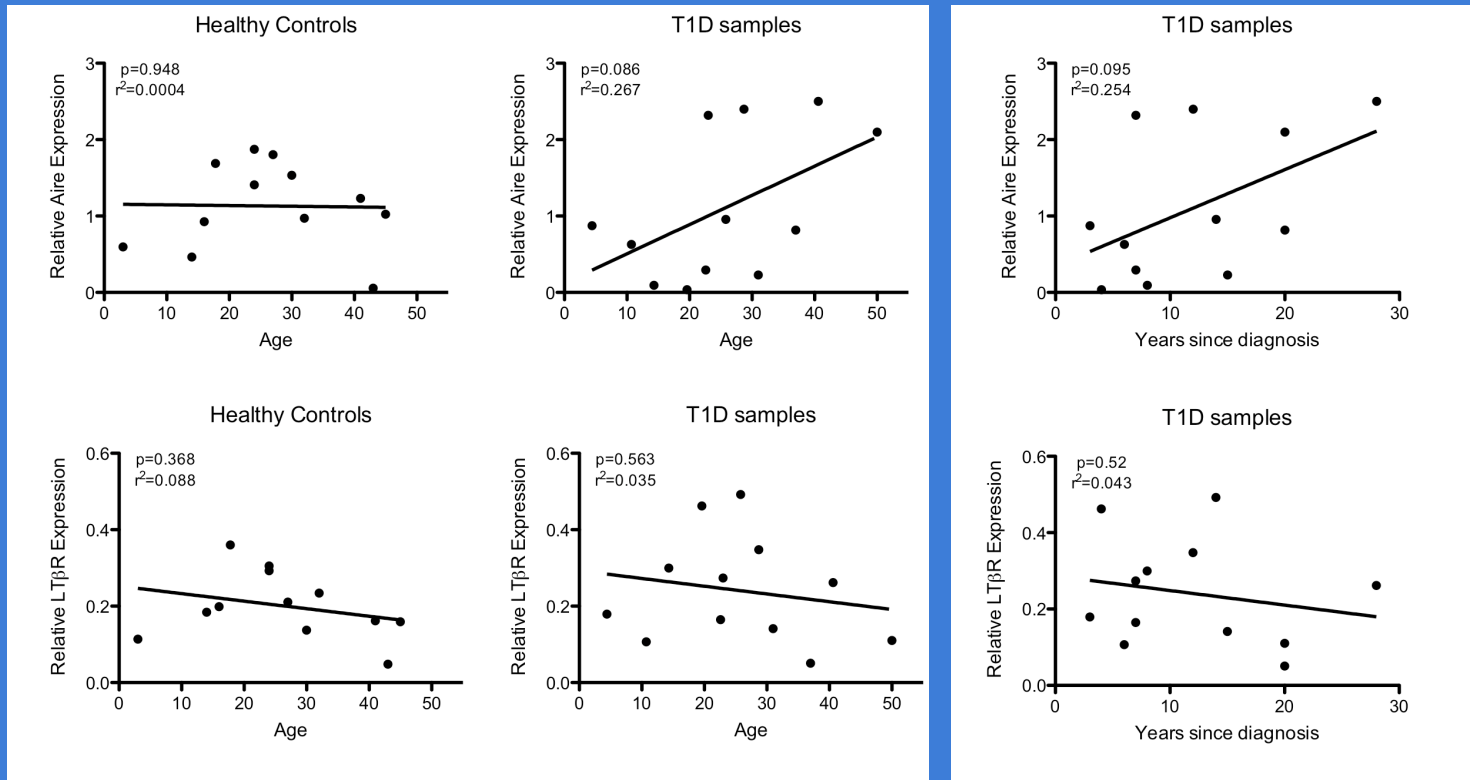


No difference in overall Aire expression

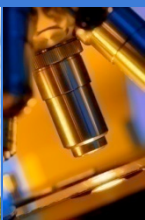


A trend for Aire expression to increase with age & years since diagnosis in T1D samples

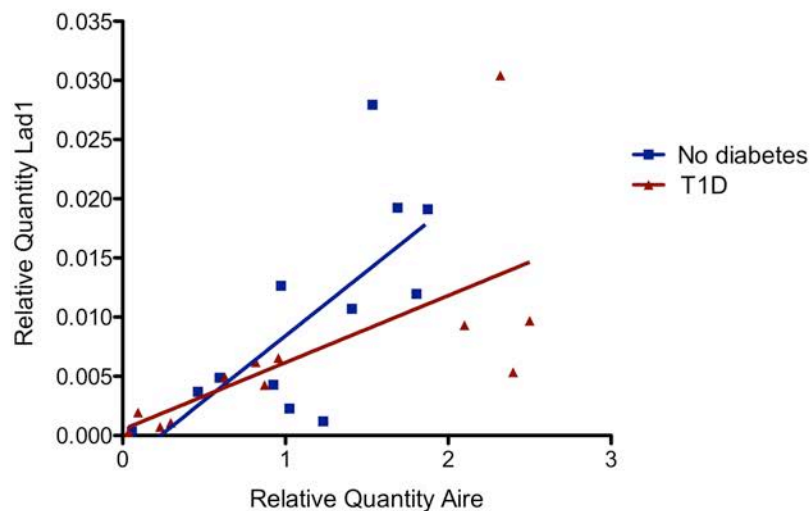
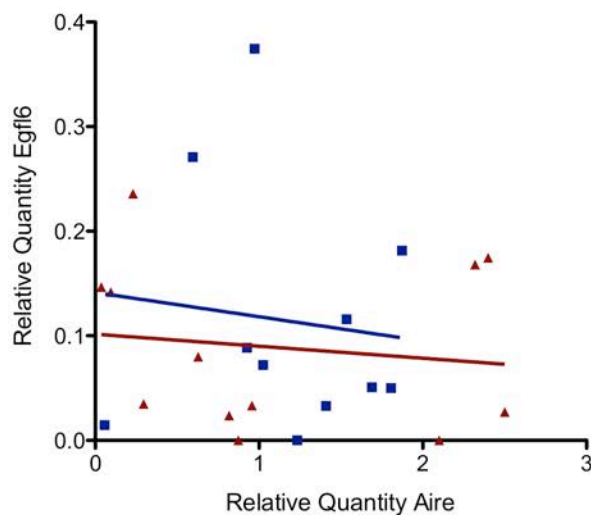
Aire



LTβR



Lad1 expression correlates with Aire expression while Egfl6 does not



Dsg1 not expressed

$p < 0.001$ for No diabetes

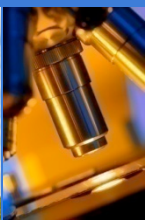
$p < 0.05$ for T1D

(no difference between T1D and no diabetes)



Future Directions

- Continue characterization of human eTACS by immunofluorescence (lineage markers & costimulatory molecules)
- Measure Aire expression levels in sorted populations from fresh LN and spleen
- Continue to improve methods of isolation, expansion, and enrichment for future functional experiments



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