Appendix 8. Heterogeneity due to first appearing autoantibody.

We recognize there is potential heterogeneity due to first appearing autoantibody, which has been shown to be predictive of unique progression patterns. We reviewed the distribution of the endotypes present in the current study population, see Table 1 below. Next, we tested for differences in each of the eigengenes that passed the filtering criteria across the autoantibody endotypes. Due to small samples size in the IA-2A and the ZnT8 groups, we combined these subgroups together. As described in Table 2 below, the difference and/or the average model eigengenes were not significantly different across the endotype groups. Further analysis with larger sample sizes and earlier measures of gene expression prior to onset of islet autoimmunity may be better suited to identify differences in gene co-expression across these autoantibody endotypes.

Appendix 8 Table 1. Reversion Incidence by First Appearing Autoantibody Pattern

	Maintainer (n=66)		**Progressor (n=25)**		**Reverter (n=47)**	
	Freq | Mean	**% | Stdev**	**Freq | Mean**	**% | Stdev**	**Freq | Mean**	**% | Stdev**
Single Autoantibody at IA						
IAA	17	25.8%	4	16.0%	17	36.2%
GADA	33	50.0%	5	20.0%	19	40.4%
ZNT8	4	6.1%	2	8.0%	6	12.8%
IA-2A	1	1.5%	3	12.0%	4	8.5%
Multiple Autoantibodies Present at IA	11	16.70%	11	44.00%	1	2.10%

Appendix 8 Table 2. Association between difference and average model eigengenes and autoantibody endotypes

	Nominal P Value
Difference Model	
Darkred	0.8012
Darkgrey	0.5967
Darkturquiose	0.8720
Darkgreen	0.1726
Lightgreen	0.7370
Average Model	
Darkolivegreen	0.8446
Paleturquoise	0.8179
White	0.1037
Yellowgreen	0.6576