

Appendix Table 1. Reversion Incidence by First Appearing Autoantibody Pattern

| | n | Number who Reverted | Reverted % | |
|---|------------|----------------------------|-------------------|----------------|
| Single Autoantibody at First Visit | | | | |
| IAA | 57 | 30 | 52.6% | |
| GADA | 72 | 31 | 43.1% | |
| ZnT8 | 11 | 4 | 36.4% | |
| IA-2A | 20 | 7 | 35.0% | |
| Multiple Autoantibodies Present at First Visit | | | | |
| | 39 | 2 | 5.1% | |
| Contrast | | | | |
| | HR* | LCL | UCL | P Value |
| GAA vs ZnT8/IA-2A | 1.07 | 0.52 | 2.19 | 0.8633 |
| IAA vs ZnT8/IA-2A | 1.88 | 0.93 | 3.79 | 0.0788 |
| Multiple vs ZnT8/IA-2A | 0.15 | 0.03 | 0.67 | 0.0133 |

*Adjusted for multiple autoantibodies at the seroconversion visit, high-risk HLA (DR3/4) genotype, non-Hispanic white ethnicity, and age at initial seroconversion, and family history of T1D.

Appendix Table 2. Unknown Metabolite Hits from GCTOF Panel†

| Metabolite | Mass to Charge [m/z] | Retention Index | HR* | Nominal P Value | FDR Adjusted P Value‡ |
|-------------------|-----------------------------|------------------------|------------|------------------------|------------------------------|
| gctof_270 | 151 | 239709 | 0.65 | 6.36E-04 | 0.1035 |
| gctof_128 | 341 | 361182 | 0.61 | 7.24E-04 | 0.1035 |
| gctof_106 | 197 | 592939 | 0.62 | 1.40E-03 | 0.1335 |
| gctof_122 | 441 | 1134692 | 1.4 | 2.74E-03 | 0.1848 |
| gctof_101 | 273 | 368671 | 0.67 | 3.23E-03 | 0.1848 |
| gctof_176 | 185 | 524969 | 0.69 | 5.55E-03 | 0.2646 |
| gctof_154 | 244 | 238992 | 0.68 | 7.00E-03 | 0.2652 |
| gctof_198 | 99 | 553406 | 0.7 | 9.99E-03 | 0.2652 |

†Hits defined as $|\text{HR}| > 1.25$ and nominal $p < 0.01$ in the single metabolite analysis, adjusted for multiple autoantibodies at the seroconversion visit, high-risk HLA (DR3/4) genotype, non-Hispanic white ethnicity, and age at initial seroconversion, and family history of T1D.

*HR represents change in hazard per 1 standard deviation increase in metabolite levels, all models are adjusted

‡False discovery rate adjusted p value

Appendix Table 3. Unknown Metabolite Hits from HILIIC Panel†

| Metabolite | Average Mass to Charge [M/Z] | Average Retention Time | HR* | Nominal P Value | FDR Adjusted P Value‡ |
|------------|------------------------------|------------------------|------|-----------------|-----------------------|
| hilic_109 | 106.09 | 5.95 | 0.61 | 4.95E-05 | 0.0511 |
| hilic_836 | 635.53 | 1.08 | 1.67 | 1.59E-04 | 0.0695 |
| hilic_267 | 235.09 | 9.97 | 0.58 | 2.02E-04 | 0.0695 |
| hilic_104 | 100.08 | 1.93 | 1.71 | 4.14E-04 | 0.1068 |
| hilic_656 | 514.87 | 1.33 | 0.62 | 1.20E-03 | 0.1917 |
| hilic_437 | 332.19 | 2.03 | 1.54 | 1.30E-03 | 0.1917 |
| hilic_179 | 173.09 | 7.35 | 0.62 | 1.98E-03 | 0.227 |
| hilic_429 | 331.05 | 9.85 | 0.62 | 2.61E-03 | 0.2612 |
| hilic_388 | 311.22 | 1.14 | 0.62 | 3.03E-03 | 0.2612 |
| hilic_348 | 294.94 | 7.64 | 0.71 | 3.19E-03 | 0.2612 |
| hilic_413 | 322.19 | 1.22 | 0.67 | 3.29E-03 | 0.2612 |
| hilic_465 | 349.02 | 9.71 | 0.65 | 4.57E-03 | 0.3017 |
| hilic_346 | 293.10 | 9.95 | 0.71 | 4.77E-03 | 0.3017 |
| hilic_669 | 522.12 | 9.39 | 1.55 | 4.83E-03 | 0.3017 |
| hilic_291 | 255.04 | 8.94 | 0.64 | 4.97E-03 | 0.3017 |
| hilic_347 | 293.25 | 9.79 | 0.67 | 5.63E-03 | 0.3228 |
| hilic_868 | 692.02 | 8.79 | 1.39 | 6.80E-03 | 0.3302 |
| hilic_277 | 244.12 | 8.18 | 0.67 | 6.87E-03 | 0.3302 |
| hilic_86 | 60.08 | 5.06 | 0.67 | 7.07E-03 | 0.3302 |
| hilic_457 | 346.01 | 8.79 | 1.5 | 7.51E-03 | 0.3302 |
| hilic_845 | 650.44 | 4.78 | 1.44 | 7.62E-03 | 0.3302 |
| hilic_266 | 235.09 | 9.87 | 0.71 | 7.95E-03 | 0.3302 |
| hilic_162 | 160.10 | 1.93 | 1.53 | 9.00E-03 | 0.3532 |
| hilic_839 | 643.48 | 1.03 | 0.76 | 9.24E-03 | 0.3532 |

†Hits defined as $|\text{HR}| > 1.25$ and nominal $p < 0.01$ in the single metabolite analysis

*HR represents change in hazard per 1 standard deviation increase in metabolite levels, all models are adjusted for multiple autoantibodies at the seroconversion visit, high-risk HLA (DR3/4) genotype, non-Hispanic white ethnicity, and age at initial seroconversion, and family history of T1D

‡False discovery rate adjusted p value

Appendix Table 4. Unknown Metabolite Hits from Lipid Panel†

| Metabolite | Mass to Charge Ratio [m/z] | Retention Time | Mode | HR* | Nominal P Value | FDR Adjusted P Value‡ |
|------------|----------------------------|----------------|----------|------|-----------------|-----------------------|
| lipid_480 | 846.67 | 6.15 | positive | 1.74 | 4.81E-05 | 0.0280 |
| lipid_797 | 1660.17 | 5.45 | negative | 1.69 | 1.90E-04 | 0.0737 |
| lipid_427 | 1156.83 | 5.02 | positive | 1.79 | 2.63E-04 | 0.0765 |
| lipid_429 | 398.77 | 5.02 | positive | 1.64 | 1.19E-03 | 0.173 |
| lipid_457 | 1162.86 | 5.48 | positive | 1.56 | 1.76E-03 | 0.2093 |
| lipid_811 | 906.89 | 6.64 | negative | 1.61 | 1.92E-03 | 0.2093 |
| lipid_266 | 577.52 | 4.83 | positive | 1.55 | 2.37E-03 | 0.2156 |
| lipid_1140 | 794.56 | 5.50 | negative | 0.64 | 2.41E-03 | 0.2156 |
| lipid_867 | 297.15 | 4.77 | negative | 1.5 | 3.41E-03 | 0.2833 |
| lipid_976 | 708.65 | 7.78 | negative | 1.49 | 3.70E-03 | 0.2869 |
| lipid_456 | 1162.36 | 5.48 | positive | 1.47 | 4.32E-03 | 0.3051 |
| lipid_937 | 561.30 | 4.77 | negative | 1.51 | 4.46E-03 | 0.3051 |
| lipid_722 | 772.59 | 6.11 | negative | 1.45 | 5.02E-03 | 0.3073 |
| lipid_809 | 859.68 | 6.43 | negative | 0.65 | 5.41E-03 | 0.3146 |
| lipid_1023 | 843.58 | 4.67 | negative | 0.69 | 6.43E-03 | 0.3561 |
| lipid_1132 | 528.31 | 1.16 | negative | 0.69 | 7.38E-03 | 0.3863 |
| lipid_993 | 763.60 | 4.88 | negative | 1.55 | 7.64E-03 | 0.3863 |
| lipid_433 | 777.55 | 5.02 | positive | 1.56 | 8.91E-03 | 0.4148 |
| lipid_739 | 950.61 | 5.52 | negative | 0.71 | 9.02E-03 | 0.4148 |

†Hits defined as |HR >1.25| and nominal p<0.01 in the single metabolite analysis

*HR represents change in hazard per 1 standard deviation increase in metabolite levels, all models are adjusted for multiple autoantibodies at the seroconversion visit, high-risk HLA (DR3/4) genotype, non-Hispanic white ethnicity, and age at initial seroconversion, and family history of T1D.

‡False discovery rate adjusted p value