|  |  |  |  |
| --- | --- | --- | --- |
| **T2D-related physiologic cluster** | **Number of   T2D-risk variants  in the cluster** | **T2D-risk variants included in the cluster  (Variant IDs)** | **Metabolic and anthropometric  features** |
| Insulin secretion 1 | 8 | rs11708067, rs505922, rs102275, rs10830963, rs1169288, rs730497, rs13266634, rs7903146 | ↑ proinsulin, ↓ FI, (↓ HOMA-B) |
| Insulin secretion 2 | 24 | rs340874, rs7633675, rs7756992, rs864745,  rs516946, rs2237895, rs5219, rs11063069,  rs4502156, rs17265513, rs35720761, rs4607103,  rs146886108, rs4457053, rs35742417, rs2191349,  rs10758593, rs10965250, rs60980157, rs5015480,  rs2237892, rs11603334, rs10842994, rs7177055 | ↓ proinsulin, ↓ FI, (↓ HOMA-B) |
| Insulin action | 16 | rs2296172, rs2943641, rs1801282, rs459193, rs972283, rs328, rs2925979, rs13389219, rs2276853, rs13133548, rs6450176, rs6905288, rs35169799, rs12602912, rs731839, rs1800961 | ↑ TG, ↑ WHR, (↑ HOMA-IR) |
| Adiposity | 6 | rs2307111, rs10146997, rs1364063, rs17782313, rs2206277, rs1558902 | ↑ BMI, ↑ WHR |
| Dyslipidemia | 3 | rs1260326, rs58542926, rs769449 | ↓ TG |
| Mix | 36 | rs140386498, rs2306374, rs35658696, rs7454108,  rs10906115, rs12571751, rs1727307, rs7202877,  rs781831, rs7501939, rs665268, rs8108269,  rs41278853, rs2412980, rs738409, rs4077129,  rs243021, rs7572857, rs4689388, rs6813195,  rs9379084, rs1361108, rs2796441, rs6585827, rs72928978, rs1531343, rs7961581, rs3764002, rs1800574, rs55834942, rs1359790, rs4886707,  rs8042680, rs2032844, rs1800437, rs4812831 | Mixed features |

**Supplemental Table 2: A summary of the six physiologic clusters that were used to construct partitioned polygenic scores for  
 T2D risk**

A total of 93 T2D-risk variants were partitioned into six distinct physiologic clusters relevant to T2D pathogenesis. Variants in each   
 physiologic cluster were associated with distinctive metabolic and anthropometric features related to T2D.

(FI = Fasting insulin; TG = Triglycerides; BMI = Body Mass Index; WHR = Waist-to-Hip ratio; HOMA-B = Homeostatic model   
 assessment for beta-cell function; HOMA-IR = Homeostatic model assessment for insulin resistance).