**Table S-26. Enrichment analysis (diabetes, type 2).**

| Annotation | Match group | FastEpistasis / logistic regression | | | | | BOOST | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N, total | N, rep. (%) | Enrich P | Min Int P | Thresh | N, total | N, rep. | Enrich P | Min Int P | Thresh |
| Exonic | None | 3248 | 2.3 | 0.615 | A: 1.02E-10<br>R: 3.11E-10 | 1.13E-12 | 3912 | 4.7 | 0.697 | A: 2.33E-11<br>R: 2.69E-11 | 1.13E-12 |
| | Either | 40 | 2.5 | | A: 2.25E-09<br>R: 4.33E-09 | 6.41E-11 | 38 | 5.3 | | A: 7.22E-09<br>R: 7.22E-09 | 6.41E-11 |
| | Both | 0 | 0 | | A: N/A<br>R: N/A | 1.46E-08 | 0 | 0 | | A: N/A<br>R: N/A | 1.46E-08 |
| Reg. 1,2, or 3 | None | 3042 | 2.4 | 0.695 | A: 1.02E-10<br>R: 3.11E-10 | 1.20E-12 | 3627 | 4.8 | 0.496 | A: 2.33E-11<br>R: 2.69E-11 | 1.20E-12 |
| | Either | 241 | 1.7 | | A: 2.30E-10<br>R: 2.76E-08 | 1.42E-11 | 317 | 3.5 | | A: 5.62E-10<br>R: 8.34E-09 | 1.42E-11 |
| | Both | 5 | 0 | | A: 4.79E-08<br>R: N/A | 6.74E-10 | 6 | 0 | | A: 2.55E-09<br>R: N/A | 6.74E-10 |
| Disease EQTL | None | 3253 | 2.3 | 0.566 | A: 1.02E-10<br>R: 3.11E-10 | 1.13E-12 | 3901 | 4.7 | 0.727 | A: 2.33E-11<br>R: 2.69E-11 | 1.13E-12 |
| | Either | 35 | 2.9 | | A: 4.48E-09<br>R: 7.68E-08 | 5.90E-11 | 49 | 2.0 | | A: 2.32E-09<br>R: 1.59E-08 | 5.90E-11 |
| | Both | 0 | 0 | | A: N/A<br>R: N/A | 1.23E-08 | 0 | 0 | | A: N/A<br>R: N/A | 1.23E-08 |
| Disease gene | None | 2610 | 2.3 | 0.833 | A: 1.02E-10<br>R: 6.27E-09 | 1.41E-12 | 3136 | 4.6 | 0.052 | A: 2.33E-11<br>R: 2.98E-10 | 1.41E-12 |
| | Either | 640 | 2.7 | | A: 1.76E-10<br>R: 3.11E-10 | 5.50E-12 | 763 | 4.5 | | A: 2.69E-11<br>R: 2.69E-11 | 5.50E-12 |
| | Both | 38 | 2.6 | | A: 5.29E-09<br>R: 3.02E-07 | 8.57E-11 | 51 | 11.8 | | A: 7.11E-10<br>R: 7.22E-09 | 8.57E-11 |
| Any gene | None | 1010 | 2.1 | 0.682 | A: 1.12E-10<br>R: 6.27E-09 | 3.74E-12 | 1252 | 4.4 | 0.297 | A: 2.33E-11<br>R: 6.40E-10 | 3.74E-12 |
| | Either | 1633 | 2.6 | | A: 1.76E-10<br>R: 3.20E-09 | 2.24E-12 | 1909 | 4.4 | | A: 2.69E-11<br>R: 2.69E-11 | 2.24E-12 |
| | Both | 645 | 2.2 | | A: 1.02E-10<br>R: 3.11E-10 | 5.35E-12 | 789 | 5.7 | | A: 2.78E-10<br>R: 4.80E-10 | 5.35E-12 |
| Marginal | None | 2857 | 2.2 | 0.439 | A: 1.02E-10<br>R: 3.11E-10 | 1.26E-12 | 3486 | 4.5 | 0.275 | A: 2.33E-11<br>R: 2.69E-11 | 1.26E-12 |
| | Either | 415 | 3.1 | | A: 3.26E-10<br>R: 1.30E-08 | 9.54E-12 | 445 | 5.6 | | A: 5.47E-11<br>R: 6.40E-10 | 9.54E-12 |
| | Both | 16 | 0 | | A: 1.45E-08<br>R: N/A | 2.89E-10 | 19 | 10.5 | | A: 1.55E-09<br>R: 6.31E-08 | 2.89E-10 |

Followed-up interactions (interactions with $P<10^{-7}$ in either the FastEpistasis or BOOST analyses) were grouped by the number of SNPs that match a particular annotation category (**Match group**: none, either, or both SNPs matching). Annotation categories are described in the Supplemental Methods section. **N, total**: total number of interactions in each annotation match group. **N, rep (%)**: percentage of the total that were nominally replicated. **Enrich P**: enrichment test P-value (testing if there is a significant difference between percentages of nominally replicated interactions among the different annotation match groups; chi-square test or Fisher's exact test). **Min Int P**: among all interactions in the particular annotation match category, the P-value of the most significant interaction (A), and the P-value of the most significant nominally replicated interaction (R). **Thresh**: hypothetical significance threshold assuming that the search space was first trimmed to only include SNP pairs corresponding to the particular annotation match group. Green shading: enrichment P-value < 0.05. Cyan shading: a "Min Int P" value that is less than the respective "Thresh".