**Supplementary Material**

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**Supplementary Method**

**To determine which eigenvectors to adjust for in association analysis:**

We evaluated the association of each eigenvector (principal component) with the outcome case-control status (**Supplementary Table 1**). The association tests suggested a significant association between pancreatic cancer outcome status and eigenvector 1, 4, 8, and 9 at *P*<0.05. There was also marginal association with eigenvector 10 (*P*=0.05). Therefore, in this study we selected the first top 10 eigenvectors for adjustment in the association testing.

**Supplementary Table 1. P-values for logistic regression of case-control status on each of the first ten eigenvectors.**

|  |  |  |
| --- | --- | --- |
| Eigenvector | P-value | Significance |
| PC1 | 2.01 × 10-13 | \*\*\* |
| PC2 | 0.49 |  |
| PC3 | 0.61 |  |
| PC4 | 2.72 × 10-4 | \*\*\* |
| PC5 | 0.11 |  |
| PC6 | 0.64 |  |
| PC7 | 0.25 |  |
| PC8 | 5.82 × 10-4 | \*\*\* |
| PC9 | 0.03 | \*\* |
| PC10 | 0.05 | . |

**Supplementary Table 2.** Sensitivity analysesfor the associations between predicted concentrations of the 38 identified proteins and pancreatic cancer risk using different subgroups

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Protein** | **PanScana I, II, III** | | **PanScana I, II** | | **PanC4b and PanScana I, II** | | **PanC4b** | | **PanC4b and PanScana I, II, III** | |
|  | OR | *P*-value | OR | *P*-value | OR | *P*-valuec | OR | *P*-value | OR | *P*-value |
| P-Selectin | 0.85 | 1.72 × 10-3 | 0.88 | 1.78 × 10-2 | 0.87 | 3.16 × 10-4 | 0.87 | 7.83 × 10-3 | 0.86 | 2.67 × 10-5 |
| Alkaline phosphatase, intestine | 0.48 | 6.10 × 10-7 | 0.56 | 1.98 × 10-4 | 0.46 | 1.41 × 10-12 | 0.39 | 6.27 × 10-10 | 0.43 | 1.91 × 10-15 |
| BGAT | 1.18 | 2.63 × 10-10 | 1.16 | 2.20 × 10-7 | 1.18 | 6.19 × 10-18 | 1.21 | 3.20 × 10-12 | 1.20 | 5.74 × 10-21 |
| C1GLC | 1.36 | 1.86 × 10-7 | 1.31 | 2.39 × 10-5 | 1.36 | 1.29 × 10-12 | 1.40 | 1.24 × 10-8 | 1.39 | 5.34 × 10-15 |
| Cadherin-5 | 1.15 | 5.26 × 10-3 | 1.17 | 3.32 × 10-3 | 1.13 | 7.20 × 10-4 | 1.10 | 5.36 × 10-2 | 1.12 | 1.10 × 10-3 |
| CD36-ANTIGEN | 1.34 | 4.17 × 10-3 | 1.39 | 2.68 × 10-3 | 1.29 | 6.66 × 10-4 | 1.21 | 5.72 × 10-2 | 1.27 | 1.01 × 10-3 |
| CRBB2 | 1.40 | 5.83 × 10-2 | 1.33 | 0.15 | 1.50 | 2.43 × 10-3 | 1.68 | 4.63 × 10-3 | 1.52 | 1.11 × 10-3 |
| Desmoglein-2 | 1.94 | 6.74 × 10-8 | 1.91 | 7.94 × 10-7 | 1.87 | 3.54 × 10-12 | 1.84 | 8.36 × 10-7 | 1.88 | 3.31 × 10-13 |
| DOCK9 | 1.25 | 5.83 × 10-2 | 1.21 | 0.15 | 1.31 | 2.43 × 10-3 | 1.41 | 4.63 × 10-3 | 1.32 | 1.11 × 10-3 |
| Endoglin | 0.44 | 1.32 × 10-6 | 0.47 | 4.88 × 10-5 | 0.43 | 1.52 × 10-11 | 0.39 | 6.86 × 10-8 | 0.41 | 2.10 × 10-13 |
| FAM3B | 1.13 | 3.21 × 10-2 | 1.10 | 0.13 | 1.14 | 3.43 × 10-3 | 1.18 | 7.29 × 10-3 | 1.15 | 8.01 × 10-4 |
| GFRAL | 1.42 | 2.77 × 10-3 | 1.47 | 2.25 × 10-3 | 1.36 | 3.43 × 10-4 | 1.26 | 5.05 × 10-2 | 1.33 | 6.15 × 10-4 |
| GLCE | 1.12 | 5.40 × 10-3 | 1.10 | 2.92 × 10-2 | 1.12 | 1.08 × 10-4 | 1.14 | 1.03 × 10-3 | 1.13 | 1.85 × 10-5 |
| IGF-IR | 0.40 | 1.32 × 10-6 | 0.44 | 4.88 × 10-5 | 0.40 | 1.52 × 10-11 | 0.36 | 6.86 × 10-8 | 0.38 | 2.10 × 10-13 |
| IL-3Ra | 0.79 | 1.06 × 10-6 | 0.81 | 4.12 × 10-5 | 0.79 | 3.72 × 10-11 | 0.78 | 2.13 × 10-7 | 0.78 | 4.80 × 10-13 |
| IR | 0.70 | 7.71 × 10-7 | 0.73 | 3.09 × 10-5 | 0.71 | 2.78 × 10-11 | 0.69 | 2.17 × 10-7 | 0.69 | 3.59 × 10-13 |
| JAG1 | 0.76 | 1.74 × 10-2 | 0.81 | 7.95 × 10-2 | 0.71 | 3.80 × 10-5 | 0.62 | 4.60 × 10-5 | 0.70 | 9.08 × 10-6 |
| LIF-sR | 0.52 | 1.32 × 10-6 | 0.55 | 4.88 × 10-5 | 0.51 | 1.52 × 10-11 | 0.48 | 6.86 × 10-8 | 0.49 | 2.10 × 10-13 |
| LMA2L | 1.36 | 2.33 × 10-2 | 1.29 | 7.68 × 10-2 | 1.37 | 2.02 × 10-3 | 1.46 | 7.36 × 10-3 | 1.39 | 6.47 × 10-4 |
| Met | 0.59 | 1.32 × 10-6 | 0.62 | 4.88 × 10-5 | 0.59 | 1.52 × 10-11 | 0.56 | 6.86 × 10-8 | 0.57 | 2.10 × 10-13 |
| Notch1 | 1.58 | 5.26 × 10-3 | 1.68 | 3.32 × 10-3 | 1.50 | 7.20 × 10-4 | 1.38 | 5.36 × 10-2 | 1.46 | 1.10 × 10-3 |
| sE-Selectin | 0.84 | 1.06 × 10-6 | 0.86 | 4.12 × 10-5 | 0.84 | 3.72 × 10-11 | 0.83 | 2.13 × 10-7 | 0.84 | 4.80 × 10-13 |
| CHST15 | 0.56 | 6.10 × 10-7 | 0.63 | 1.98 × 10-4 | 0.55 | 1.41 × 10-12 | 0.48 | 6.27 × 10-10 | 0.52 | 1.91 × 10-15 |
| STOM | 1.15 | 6.80 × 10-2 | 1.12 | 0.17 | 1.19 | 2.17 × 10-3 | 1.26 | 3.36 × 10-3 | 1.19 | 1.05 × 10-3 |
| TENC1 | 1.20 | 5.83 × 10-2 | 1.16 | 0.15 | 1.24 | 2.43 × 10-3 | 1.31 | 4.63 × 10-3 | 1.25 | 1.11 × 10-3 |
| THSD1 | 0.77 | 3.07 × 10-3 | 0.77 | 7.31 × 10-3 | 0.73 | 1.84 × 10-6 | 0.71 | 8.90 × 10-5 | 0.74 | 5.85 × 10-7 |
| TLL1 | 1.38 | 5.26 × 10-3 | 1.43 | 3.32 × 10-3 | 1.33 | 7.20 × 10-4 | 1.25 | 5.36 × 10-2 | 1.30 | 1.10 × 10-3 |
| TM11D | 1.14 | 5.83 × 10-2 | 1.11 | 0.15 | 1.16 | 2.43 × 10-3 | 1.22 | 4.63 × 10-3 | 1.17 | 1.11 × 10-3 |
| ADH1B | 1.16 | 7.87 × 10-2 | 1.14 | 0.16 | 1.21 | 2.30 × 10-3 | 1.29 | 3.71 × 10-3 | 1.22 | 1.28 × 10-3 |
| B3GN2 | 1.91 | 1.06 × 10-6 | 1.79 | 4.12 × 10-5 | 1.90 | 3.72 × 10-11 | 2.00 | 2.13 × 10-7 | 1.97 | 4.80 × 10-13 |
| CHSTB | 3.43 | 1.52 × 10-10 | 2.98 | 1.04 × 10-7 | 3.41 | 5.42 × 10-18 | 3.86 | 6.87 × 10-12 | 3.62 | 5.57 × 10-21 |
| DC-SIGN | 1.30 | 2.63 × 10-10 | 1.26 | 2.20 × 10-7 | 1.30 | 6.19 × 10-18 | 1.35 | 3.20 × 10-12 | 1.32 | 5.74 × 10-21 |
| GP116 | 0.77 | 1.06 × 10-6 | 0.79 | 4.12 × 10-5 | 0.77 | 3.72 × 10-11 | 0.76 | 2.13 × 10-7 | 0.76 | 4.80 × 10-13 |
| gp130, soluble | 0.74 | 5.70 × 10-3 | 0.71 | 3.86 × 10-3 | 0.72 | 4.43 × 10-5 | 0.74 | 5.24 × 10-3 | 0.73 | 2.94 × 10-5 |
| IP-10 | 0.86 | 0.14 | 0.82 | 7.27 × 10-2 | 0.77 | 5.73 × 10-4 | 0.72 | 2.26 × 10-3 | 0.79 | 1.19 × 10-3 |
| sTie-2 | 1.36 | 4.17 × 10-3 | 1.41 | 2.68 × 10-3 | 1.30 | 6.66 × 10-4 | 1.22 | 5.72 × 10-2 | 1.28 | 1.01 × 10-3 |
| VEGF sR2 | 0.82 | 4.34 × 10-4 | 0.84 | 4.88 × 10-3 | 0.82 | 1.32 × 10-6 | 0.79 | 6.54 × 10-5 | 0.80 | 4.86 × 10-8 |
| F177A | 0.66 | 1.41 × 10-4 | 0.73 | 7.36 × 10-3 | 0.65 | 5.58 × 10-8 | 0.58 | 1.14 × 10-6 | 0.63 | 1.54 × 10-9 |