

## **Blood cells of high risk pancreatic cancer subjects with pancreatic lesions detectable in MRI display a methylation signature detectable also in blood of PDAC patients**

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### **Background:**

Pancreatic ductal adenocarcinoma (PDAC) is highly lethal, with a post-diagnosis median survival of 4.6 months and majority of cases are diagnosed at advanced stages. First-degree relatives of PDAC patients carry at least a two-times higher risk of this cancer and known germline mutations (e.g. in *BRCA1*) explain only 5–10% of cases. The environmental factors associated with PDAC include, for instance, type-2-diabetes, chronic pancreatitis, and

smoking but none of these factors was predominantly associated with this cancer. Detection of the individuals with elevated-risk of PDAC, as well as early detection of this neoplasm, are crucial to improve outcomes of this disease, but remain inadequate.

### **Materials and methods:**

We profiled blood DNA methylation of 169 healthy subjects with elevated PDAC risk who received whole-body MRI (WB-MRI) and of 24 sporadic PDAC cases using InfiniumMethylationEPIC v2.0. Across the study participants, WB-MRI detected suspicious lesions (ONCORADS 3-5) in 46 subjects including: 20 with pancreatic lesions and 26 with lesions involving other organs. For the remaining 123 individuals, MRI showed no abnormalities or benign (ONCORADS 2) lesions. All study participants underwent assessment of epidemiological PDAC risk score based on 32 environmental factors previously associated with PDAC.

### **Results:**

Using a 32-factor epidemiological risk score as a covariate, we found four CpG sites with statistically significant hypomethylation in the blood of individuals with suspicious lesion in pancreas visible on MRI. These changes were also present in blood of 24 PDAC cases.

### **Conclusions:**

In conclusion, individuals with suspicious pancreatic lesions exhibit blood methylation changes with potential utility in PDAC risk assessment.

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