World Academy of Science, Engineering and Technology
International Journal of Bioengineering and Life Sciences
Vol:18, No:02, 2024

ScRNA-Seq RNA Sequencing-Based Program-Polygenic Risk Scores Associated with Pancreatic Cancer Risks in the UK Biobank Cohort

Authors : Yelin Zhao, Xinxiu Li, Martin Smelik, Oleg Sysoev, Firoj Mahmud, Dina Mansour Aly, Mikael Benson

Abstract : Background: Early diagnosis of pancreatic cancer is clinically challenging due to vague, or no symptoms, and lack of biomarkers. Polygenic risk score (PRS) scores may provide a valuable tool to assess increased or decreased risk of PC. This study aimed to develop such PRS by filtering genetic variants identified by GWAS using transcriptional programs identified by single-cell RNA sequencing (scRNA-seq). Methods: ScRNA-seq data from 24 pancreatic ductal adenocarcinoma (PDAC) tumor samples and 11 normal pancreases were analyzed to identify differentially expressed genes (DEGs) in in tumor and microenvironment cell types compared to healthy tissues. Pathway analysis showed that the DEGs were enriched for hundreds of significant pathways. These were clustered into 40 “programs” based on gene similarity, using the Jaccard index. Published genetic variants associated with PDAC were mapped to each program to generate program PRSs (pPRSs). These pPRSs, along with five previously published PRSs (PGS000083, PGS000725, PGS000663, PGS000159, and PGS002264), were evaluated in a European-origin population from the UK Biobank, consisting of 1,310 PDAC participants and 407,473 non-pancreatic cancer participants. Stepwise Cox regression analysis was performed to determine associations between pPRSs with the development of PC, with adjustments of sex and principal components of genetic ancestry. Results: The PDAC genetic variants were mapped to 23 programs and were used to generate pPRSs for these programs. Four distinct pPRSs (P1, P6, P11, and P16) and two published PRSs (PGS000663 and PGS002264) were significantly associated with an increased risk of developing PC. Among these, P6 exhibited the greatest hazard ratio (adjusted HR[95% CI] = 1.67[1.14-2.45], p = 0.008). In contrast, P10 and P4 were associated with lower risk of developing PC (adjusted HR[95% CI] = 0.58[0.42-0.81], p = 0.001, and adjusted HR[95% CI] = 0.75[0.59-0.96], p = 0.019). By comparison, two of the five published PRS exhibited an association with PDAC onset with HR (PGS000663: adjusted HR[95% CI] = 1.24[1.14-1.35], p < 0.001 and PGS002264: adjusted HR[95% CI] = 1.14[1.07-1.22], p < 0.001). Conclusion: Compared to published PRSs, scRNA-seq-based pPRSs may be used not only to assess increased but also decreased risk of PDAC.

Keywords : cox regression, pancreatic cancer, polygenic risk score, scRNA-seq, UK biobank
Conference Title : ICCB 2024 : International Conference on Cancer Bioinformatics
Conference Location : Amsterdam, Netherlands
Conference Dates : February 05-06, 2024