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Construction of cancer pathways for personalized medicine

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We describe approach to infer pathways activated in tumors from individual gene expression profiling data of cancer patients. Tumor microarray expression data is imported into Pathway Studio software, normalized on normal tissue, and analyzed by sub-network enrichment analysis (SNEA) option "Expression targets" to identify major regulators up-stream of differentially expressed genes. We then compare regulators found by software with the collection of cancer-related pathways developed in Pathway Studio. This pathway collection is based on SNEA regulators identified in previously analyzed cancer patients. Our collection currently has 47 cancer-related pathways describing biological processes frequently activated during tumorogenesis: cell cycle, apoptosis, angiogenesis, epithelial-to-mesenchymal transition, macrophage activation, and neutrophil infiltration. Pathways contain 3,674 proteins and are gradually improved by adding new SNEA regulators from new patients. More than 50% of expression profiles from new patients can be explained by existing pathway collection. We find that majority of advanced solid tumors are characterized by macrophage activation through apoptotic clearance, angiogenesis and EMT induced by hypoxia due to venous thrombosis. Our approach allows quick identification of key processes and regulators responsible for tumor growth in a given patient. We propose that major expression regulators identified by SNEA in patient tumor can be considered as potential targets for therapeutic intervention. Information about drugs inhibiting SNEA regulators is readily available in Pathway Studio. With our cancer pathway collection Pathway Studio becomes one-stop knowledgebase for designing personalized drug treatment based on patient gene expression profile.

Biography

Anton Yuryev received his PhD at Johns Hopkins University where he discovered proteins physically linking RNA polymerase II transcription and RNA processing in eukaryotic cells. At birth of Bioinformatics he began working on sequence and genotyping analysis as Senior Scientist at InforMax, continued at Orchid Bioscience as Senior Bioinformatics Analyst to optimize primer design, and then at Ariadne Genomics developing new approaches for pathway and network analysis. He has published over 40 scientific publications, edited 3 scientific books. He is now the Director of Professional services at Elsevier.

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