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Correlation between the expression of embryonic master regulators SOX9 and PDX1 in pancreatic cancer samples

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The process of embryonic gene recapitulation can be commonly observed during cancer progression. Identification of the factors involved in embryogenesis can reveal important regulators of carcinogenesis. The transcription factors SOX9 and PDX1 are most important master regulators of pancreas development. Cooperation of these factors is required to determine the direction of pre-pancreatic cell differentiation in early embryogenesis. At early stages of pancreatic endoderm differentiation, SOX9 expression coincides with the appearance of PDX1 expression. To upregulate each other's expression, PDX1 and SOX9 should act reciprocally. PDX1 expression has been identified in precursor lesions of pancreatic cancer. Persistent expression of PDX1 in the pancreas causes acinar-to-ductal metaplasia (ADM) that is crucial for the origin of PDAC. SOX9 expression in Kras-activated acinar cells causes ADM progressing to a duct-like state and PanIN/PDAC. In this study, we directly compared the SOX9 and PDX1 expression levels in pancreatic cancer samples (n=40) and normal pancreas samples (n=12). Tumor samples were divided into three groups according to the level of SOX9 expression. The first group showed a 6.5-fold increased expression level with respect to the normal one ($p=2*10.5$). The second and normal groups had approximately equal levels of SOX9 expression. The third group showed a 25-fold decreased expression level ($p=10.5$). A similar trend to such grouping was also characteristic of PDX1 expression. The correlation coefficient between SOX9 and PDX1 levels was 0.7 ($p<10.5$). There was no correlation between the levels of SOX9 or PDX1 and the extent of cancer cell differentiation. The gene expression heterogeneity observed can be linked to a change in the gene function during tumor progression. The correlation between PDX1 and SOX9 in cancer samples may indicate the participation of these factors in the regulatory module. This study was supported by the Russian Science Foundation (project no. 14-50-00131).

Recent Publications:

1. Kondratyeva L G, Chernov I P, Zinovyeva M V, Kopantzev E P and Sverdlov E D (2017) Expression of master regulatory genes of embryonic development in pancreatic tumors. Doklady Biochemistry and Biophysics 475(1):250–252.
2. Kondratyeva L G, Didych D A, Chernov I P, Kopantzev E P, Stukacheva E A, et al. (2017) Dependence of expression of regulatory master genes of embryonic development in pancreatic cancer cells on the intracellular concentration of the master regulator PDX1. Doklady Biochemistry and Biophysics 475(1):259–263.
3. Kondratyeva L G, Kashkin K N, Chernov I P, Stukacheva E A, Dydich D A, et al. (2017) PCNA: a constitutive human promoter for gene expression for functional studies and therapeutic applications. Molecular Genetics, Microbiology and Virology 32(3):137–140.
4. Zinovyeva M V, Kostina M B, Chernov I P, Kondratyeva L G and Sverdlov E D (2016) KLF5, a new player and new target in the permanently changing set of pancreatic cancer molecular drivers. Russian Journal of Bioorganic Chemistry 42(6):606–611.
5. Kondratyeva L G, Vinogradova T V, Chernov I P and Sverdlov E D (2015). Master transcription regulators specifying cell-lineage fates in development as possible therapeutic targets in oncology. Russian Journal of Genetics 51(11):1049–1059.

Biography

Liya G Kondratyeva is currently in her final year of Post-graduation at the Laboratory of Human Gene Structure and Function at the Institute of Bioorganic Chemistry, RAS. Her research project is devoted to the genetic study of pancreatic ductal adenocarcinoma, which is the most widely spread and extremely aggressive type of cancer.

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