TRANSCRIPTOME PROFILING BY NEXT-GENERATION SEQUENCING AND PATHWAY ANALYSIS OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA IN KAZAKHSTAN.

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Introduction. Esophageal cancer is the eighth most common cancer in the world and the highest in Eastern Asia. The incidence rate in Kazakhstan is 10.1: 100 000. Esophageal squamous cell carcinoma (ESCC) is the dominant histological type (> 90%) of esophageal cancer cases. Usage of NGS technologies allows determining effective diagnostic markers and therapeutic approaches for to increase the longevity of the patients. The aim of the project is to identify genetic basis of ESCC by performing whole transcriptome sequencing in Kazakhstani patients.

Materials and Methods. Eleven patients with ESCC underwent surgery at Oncology center (Astana, Kazakhstan) between June and December 2013. Fresh frozen cancer and its adjacent normal tissue specimen were obtained from each patient (in total 11 tumor center samples and 11 normal tissue samples). Whole transcriptome sequencing was performed on Illumina HiSeq2000 platform using TruSeq RNA protocol. TopHat2 and DeSeq have been used for mapping and defining of differentially expressed genes, correspondingly. MSigDB and KEGG databases were processed for analysis of signaling networks.

Results. Paired analysis of cancer and normal tissues identified 287 down-regulated and 192 up-regulated genes. Among up-regulated genes PPAR signaling pathway (p value=0.01), cytokine-cytokine receptor interaction (p value=0.05) and metabolism of lipids and lipoproteins (p value=0.03) have been identified. Whereas the most significant pathways among down-regulated genes are metabolism of xenobiotics by cytochrome P450 (p value=1.31E-4), retinol metabolism P450 (p value=0.01), O-Glycan biosynthesis (p value=0.02).

Conclusion. High-throughput sequencing approach allows identifying molecular pathways involved in esophageal carcinogenesis that could improve diagnosis and treatment strategies.