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Computer analysis of genes associated with Kaposi's sarcoma

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Motivation and Aim: Kaposi's sarcoma is a cancer that develops from cells that line the lymph or blood vessels [1]. It usually appears as tumors on the skin or mucosal surfaces (inside the mouth), but these tumors can also develop in other parts of the body, such as the lymph nodes (bean-sized clusters of immune cells throughout the body), the lungs, or the digestive tract. It is important to describe new target genes for this disease. We aimed reconstruct gene network for future development of novel therapeutics or repurposing of existing treatment strategies, particularly in identifying new biomarkers as hub genes in such network.

Methods and Algorithms: We used open bioinformatics tools and databases following the approaches for gene network reconstruction and analysis presented in [2, 4]. The task is to build (collect) a list of genes associated with the development of Kaposi's sarcoma, analyze the categories of gene ontologies for such a list, and reconstruct the gene network. First, we constructed the list of genes associated with a hereditary predisposition to Kaposi's sarcoma. The Internet-resource OMIM (Online Mendelian Inheritance in Man) (https://omim.org/) was used to analyze the genes. A search for the keyword Kaposi sarcoma (Kaposi's sarcoma) gave 273 genes - ACTFS, ACTG2, ADSL, ALKBH1, etc. We used also GeneCards.org platform for the annotation of sarcoma genes. Next step is estimation of enriched gene ontologies categories in the gene list and gene network reconstruction. The PANTHER resources (Protein Analysis THrough Evolutionary Relationships) (http://pantherdb.org/) were used to analyze the categories of gene ontologies.

Results: The most significant categories for Kaposi's sarcoma genes were regulation of metabolic processes of the connection of nitrogen and macromolecules, regulation of the cellular metabolic process, regulation of cell proliferation, regulation of the process of biosynthesis and the metabolic process of RNA. Next, the categories of gene ontologies for molecular functions were calculated. The most significant categories are heterocyclic binding, organic cyclic binding, protein binding, and to a lesser extent specific DNA binding. Further, similarly, with the help of PANTHER, an ontology table for cellular components was built. The most significant categories for Kaposi's sarcoma genes are the nucleoplasm, nucleus, nuclear chromosome, chromatin, intracellular non-membrane organelles (ribosomes). Thus, PANTHER for Kaposi's sarcoma genes confirm the categories of gene ontologies of protein binding, nuclei, non-membrane organelles, metabolic processes, and RNA biosynthesis. The most significant categories for this list of genes include the regulation of metabolic processes, cell proliferation, and transcriptional disruption in cancer.

GeneMANIA (https://genemania.org/) and STRING-DB (https://string-db.org/) resources were used to reconstruct the gene network of interactions between Kaposi's sarcoma genes. In the center of the network are Kaposi's sarcoma genes that have a large number of connections with other elements – MYC, TP53, CDKN1A. From STRING-DB it can be found that the network is quite sparse, some objects (proteins) do not contact with others. A central, strongly connected cluster of genes stands out. In total, 214 genes from the list were recognized by STRING-DB tool. The network has a non-randomly large number of connections (at level $p < 1.0e-16$), the average degree of network node (protein) connectivity is 12.7, and the clustering coefficient is 0.501. There are several clusters of the network – the largest one includes the genes HARS, KRAS, NRAS, PTPN11. There are several smaller, but also connected in a common network of clusters, the largest number of links in the TP53 gene (a known oncogene). In general, analysis of the structure of the gene network for SC genes shows the existence of a dense, connected, rather large cluster of genes (network nodes) that includes known oncogenes, such as TP53.

Conclusion: Kaposi's sarcoma is a dangerous disease, but with a fairly high survival rate [5]. Treatment for Kaposi's sarcoma can be local or systemic. Local therapy includes applications of 30 % prospidin ointment, radiation methods, cryotherapy, injections of chemotherapeutic drugs into the tumor, applications with dinitrochlorobenzene, injections of interferon-alfa into the tumor, and some other methods [7]. Radiation therapy, local chemotherapy, surgical method, cryotherapy with liquid nitrogen, photodynamic therapy, systemic polychemotherapy or palliative monochemotherapy approaches also used [6]. The study of the structure of the gene network shows a high connectivity of genes and their products. An analysis of the literature (PubMed) showed a continuing increase in publications on this topic – a total of 11,800 publications to date. There are new approaches based on circular RNA studies [3].

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