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A Comprehensive Study of Possible Crosstalk between Angiogenic and Metabolic Signaling Pathways in Cancer

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Abstract

Purpose:

Tumor angiogenesis is a fundamental, complex and dynamic process necessary for the growth of solid tumors. Vascular system is a highly branched network lined by endothelial cells (ECs), it supplies tissues with oxygen (O2) and nutrients. During angiogenesis, ECs must increase associated metabolic activities to facilitate incorporation of nutrients into biomass. Understanding EC metabolism reveals new perspectives on disease mechanisms in the vascular system and provides new therapeutic approaches for disorders complicated with aberrant vessel growth. Metabolic pathways, such as glycolysis, play distinct, essential roles during vessel formation. In adults, most ECs are quiescent for extended periods, however, they rapidly switch to growth upon proangiogenic stimulation. Signaling pathways that control angiogenic switch control EC metabolism, eliciting a metabolic state permissive for growth and proliferation. Interfering with these metabolic adaptions renders ECs less sensitive to angiogenic signals. Another compensatory mechanism to hypoxia is metabolic symbiosis, a process in which cells in the oxygenated milieu use lactate to produce ATP, which is associated with the activation of glycolytic genes. The aim of this study is network analysis of known angiogenic pathways and related metabolic signaling pathways, looking for their intrinsic communication and determine plausible bottlenecks as novel targets in cancer disease.

Methods:

We investigated the association between angiogenesis, metabolic symbiosis and endothelial cell metabolic pathways using protein-protein interaction, gene-gene interaction and text mining approach by bioinformatics tools. By recruiting the markers of angiogenesis, metabolic symbiosis and endothelial cell metabolism in AMD, we designed an intersection network that includes information on how these three biological phenomena are linked.

Results:

We selected 92 important genes from multiple signaling pathways. The network of those genes was visualized using the Cytoscape software, highly interconnected regions (clusters), hub nodes with the highest degree-and nodes which control most of the information flow- in the network were identified by using Molecular Complex Detection (MCODE) and centrality analysis respectively.

Conclusion:

The results are leading us to the promising new directions in revealing cancer mechanisms and development of possible new treatment.

Keywords:

Crosstalk,

Angiogenic,

Metabolic,

Cancer.