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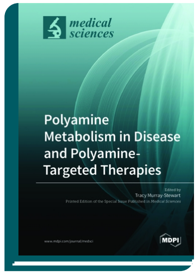
Special Issue Reprint

Polyamine Metabolism in Disease and Polyamine-Targeted Therapies



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Polyamines are ubiquitous polycations essential for all cellular life. The most common polyamines in eukaryotes, spermine, spermidine, and putrescine, exist in millimolar intracellular concentrations that are tightly regulated through biosynthesis, catabolism, and transport. Polyamines interact with, and regulate, negatively charged macromolecules, including nucleic acids, proteins, and ion channels. Accordingly, alterations in polyamine metabolism affect cellular proliferation and survival through changes in gene expression and transcription, translation, autophagy, oxidative stress, and apoptosis. Dysregulation of these multifaceted polyamine functions contribute to multiple disease processes, thus their metabolism and function have been targeted for preventive or therapeutic intervention. The correlation between elevated polyamine levels and cancer is well established, and ornithine decarboxylase, the rate-limiting biosynthetic enzyme in the production of putrescine, is a bona fide transcriptional target of the Myc oncogene. Furthermore, induced polyamine catabolism contributes to carcinogenesis that is associated with certain forms of chronic infection and/or inflammation through the production of reactive oxygen species. These and other characteristics specific to cancer cells have led to the development of polyamine-based agents and inhibitors aimed at exploiting the polyamine metabolic pathway for chemotherapeutic and chemopreventive benefit. In addition to cancer, polyamines are involved in the pathologies of neurodegenerative diseases including Alzheimer's and Parkinson's, parasitic and infectious diseases, wound healing, ischemia/reperfusion injuries, and certain age-related conditions, as polyamines are known to decrease with age. As in cancer, polyamine-based therapies for these conditions are an area of active investigation. dvances in immunotherapy, interest has increased regarding polyamine- odulation of immune responses, as well as potential immunoregulation of tabolism, the results of which could have relevance to multiple disease processes. The goal of this Special Issue of Medical Sciences is to present the most recent advances in polyamine research as it relates to health, disease, and/or therapy.

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