Overexpression of JAK3 in Coronary Arteries of Kawasaki Disease Patients Reveals a New Potential Therapeutic Target

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Kawasaki Disease (KD) is a febrile illness predominantly affecting children under five years old and is the leading cause of acquired heart disease in children in developed countries. If KD is not diagnosed and treated on time, it can result in inflammation of coronary arteries (CA) and ultimately a fatal CA aneurysm. This inflammatory process is why KD is deadly, yet much of the KD immune response is unknown. This research sought to identify overexpressed immune proteins in KD CA to gain insight into the KD immune response and determine future targets of treatment. After examining RNA-sequencing results from a previous study, four genes were identified as upregulated in KD CA: Cluster of Differentiation 69 (CD69), Cluster of Differentiation 96 (CD96), Janus Kinase 3 (JAK3), and Integrin Subunit Alpha L (ITGAL). CA tissues from 8 fatal child KD cases and 8 fatal non-KD child controls were stained using immunohistochemistry to detect if high gene expression of CD69, CD96, JAK3, and ITGAL translated into high protein expression in KD patients. Using the Wilcoxon Rank-Sum Test for visual analysis of slides (JAK3: $p=0.0013$) and logistic regression for ImageJ stain quantification (JAK3: $p=0.008$), JAK3 was the only protein in both analyses with significantly high expression in KD CA inflammatory cells. Therefore, JAK3 is proposed as a potential KD therapeutic target. JAK3 inhibitors are already employed in treatment for inflammatory illnesses like rheumatoid arthritis, warranting further studies on its application in KD patients unresponsive to current therapies. This research further elucidates the KD immune response by identifying JAK3 as a significantly upregulated protein in the KD immunologic response and proposing JAK3 as a specific target to investigate for KD therapy.

Awards Won:
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