SHP2 increases robustness and information transfer within IL-6-induced JAK/STAT signalling

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Abstract

Dysregulation of the IL-6-induced JAK/STAT cascade is associated with severe inflammatory and proliferative diseases. The cascade is normally tightly controlled by proteins such as the feedback inhibitor SOCS3 and the tyrosine phosphatase SHP2. SOCS3 increases the stability of late IL-6-induced STAT3 activation across cells with different STAT3 levels and reduces the signal magnitude. but whether SHP2 similarly affects robustness and information transfer remains unclear. Researchers recently used multiplexed single-cell analyses and information theory approaches to clarify SHP2's roles. They found that SHP2 improved the robustness of STAT3 activation under basal conditions (in the absence of the cytokine IL-6) and during early IL-6 signalling levelling the degree of activation across cells with heterogeneous expression levels of STAT3. However, it did not affect the robustness of late IL-6-induced STAT3 activation. In contrast to SOCS3, SHP2 increased information transfer through the IL-6-induced cascade, probably by reducing basal activation "noise" and thereby increasing the sensitivity of the cells to IL-6-mediated activation. Although further research is needed, the results increase understanding of the functions of SHP2 in the critical JAK/STAT pathway and provide insights that may aid the development of treatments for diseases related to JAK/STAT overactivation.