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Dissection of the Dictyostelium STAT activation pathways: Just Another Kinase for a non-metazoan STAT

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Phosphotyrosine signalling pathways regulate many cellular functions. In metazoans, STAT (Signal Transducer and Activator of Transcription) plays an important role in immune system. The tyrosine kinase JAK (Janus Kinase or Just Another Kinase) controls STAT activation. The cellular slime mold *Dictyostelium discoideum* is the only non-metazoan organism with functionally characterised SH2 (phosphotyrosine binding) domains but tyrosine kinases are unknown. *Dictyostelium* STATc protein is rapidly tyrosine-phosphorylated when cells are treated with the polyketide DIF-1 (Differentiation Inducing Factor-1) or exposed to hyper-osmotic stress. We show that STATc has a novel mode of activation, whereby DIF-1/stress induced serine phosphorylation of the protein tyrosine phosphatase results in the inhibition of its activity, shifting the phosphorylation-dephosphorylation equilibrium in favour of phosphorylation. Also, we have recently identified two TKL (tyrosine kinase-like) proteins as STATc activating kinases. TKL group kinases exist in almost all eukaryotes and are mainly classified as serine/threonine kinases. "STAT activation by PTP inhibition" and "STAT tyrosine phosphorylation by TKL"; these findings suggest a novel, possibly ancient, STAT regulation mechanism.

学外の方の聴講歓迎・申込不要・参加無料

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