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Functional interaction of the TRIM8/GERP ring finger protein with PIM serine/threonine kinases

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The E3 ubiquitin ligase TRIM8 has been initially identified as a Ring finger protein expressed in glioblastomas capable of binding SOCS-1, a member of the Suppressor of Cytokine Signaling family of molecules. It has been reported by us that TRIM8 appears to be a negative regulator of SOCS-1 stability by binding to its SH-2/SOCS box domains. Moreover, recent reports have documented that nucleocytoplasmic trafficking of TRIM8 is involved in positive regulation of TNF- α induced NF- κ B activation, in the stabilization of p53 on glioblastoma and clear cell renal carcinoma, and in the degradation of PIAS the negative regulator of STAT3. Here, we show for the first time that PIM serine/threonine kinases, also bind and phosphorylate TRIM8, resulting in increased stabilization of the ubiquitin ligase activity. Since SOCS-1 is functionally phosphorylated and also stabilized by PIMs, co-expression of a heterotrimeric TRIM8/SOCS-1/PIM complex promotes partial destabilization of the complexes and pursues degradation of the SOCS-1 protein. Additionally, co-expression of SOCS-1/TRIM8/PIM kinase complexes in 293T cells mitigates the repression of an interferon- γ -mediated signaling in responsive cells *in vivo*. These data add new partners to the complex network of protein-protein interactions that regulate SOCS-1 function and modulate the cytokine biological response. (Up to 250 words)

Biography

De Iuliis has completed his Medical School at the age of 25 years from Chieti University, Chieti, Italy. On 2013 He was accepted as a Resident in Clinical Pathology, SS Annunziata University Hospital, University of Chieti and as a postdoctoral fellow in the Department of Medical, Oral and Biotechnology Sciences. Currently he is developing bio-medical projects related to the biochemical mechanisms undergoing autophagy and apoptosis on established tumor cells. Please refer to Pubmed for his first paper as first author. In addition he has two papers in press as a first author and has submitted other five manuscripts.

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