Mimetics of SOCS proteins as antinflammatory therapeutics in cancer

Inflammation is a critical component of tumor progression indeed the tumor microenvironment is largely orchestrated by inflammatory cells and tumor cells have adopted some of the signalling molecules of the innate immune system, as chemokines and their receptors for invasion, migration and metastasis. Janus Kinase-Signal Transducer and Activator of Transcription (JAK-STAT) signaling mediates almost all immune regulatory processes, including those that are involved in tumor cell recognition and tumor-driven immune escape. The ability of Suppressor of Cytokine Signaling (SOCS) proteins to modulate JAK/STAT effects suggest them as attractive templates for immunotherapeutics design. Lung and breast cancers have dramatic spreading features and many studies reported that in them the downregulation of two SOCS members, SOCS1 and 3 is associated with tumor progression and metastatization. Furthermore restoration of SOCS1,3 proteins, through recombinant methods or demethylation drugs, in these tumors demonstrated to inhibit the colony growth and metastasis in breast cancer of and serve as a potential strategy for antitumor therapy. In this project, proteomimetics of SOCS1 and 3 will be investigated: starting from design, chemical synthesis to in vitro functional and structural characterization and optimization. Subsequently, a further prioritization phase of new compounds will be based on cellular assays that will provide few therapeutics to be preliminary tested *in vivo*. To reach these goals, a multidisciplinary approach will be employed: i) Design and characterization of mimetic compounds of SOCS 1 and 3: biochemical in vitro binding assays and SAR investigations, also through NMR studies, ii) optimization of nanoparticles for cellular delivery for entire SOCS proteins and their proteomimetics to obtain specific antitumor compounds as mimetics of natural inhibitors of JAK-STAT.

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