Effect of post-translational modifications on the behavior of stimulated STAT3-GRIM19 heterodimers

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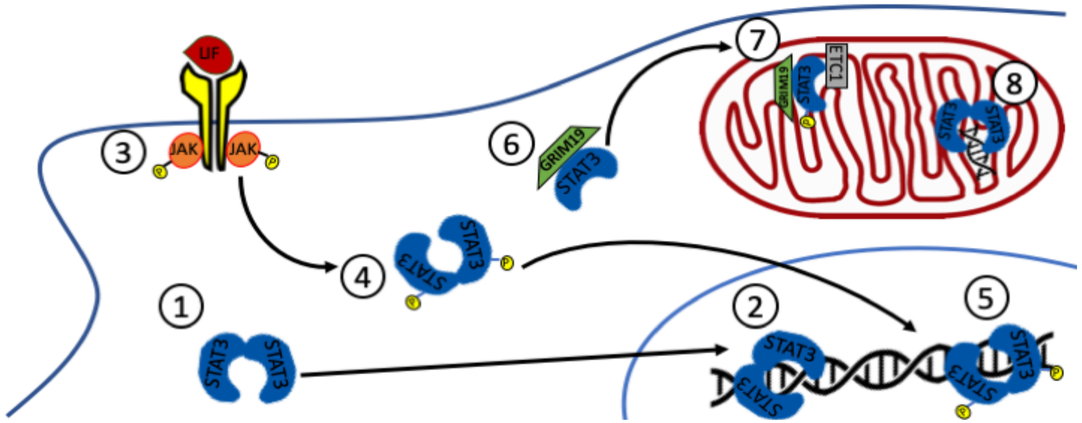
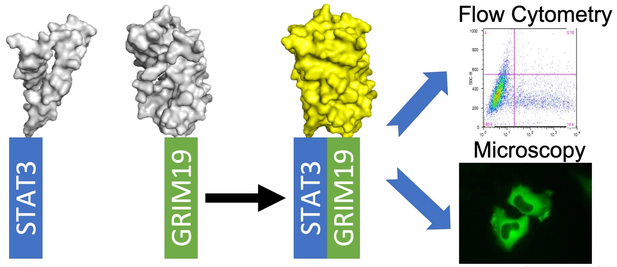
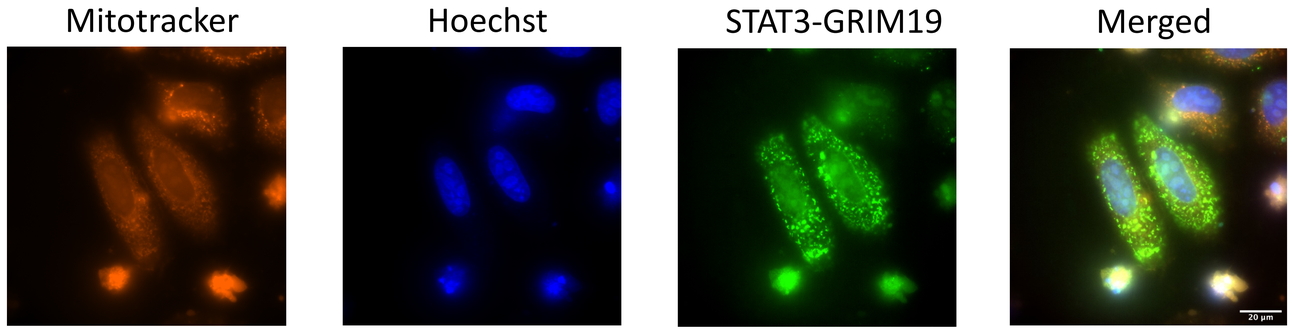


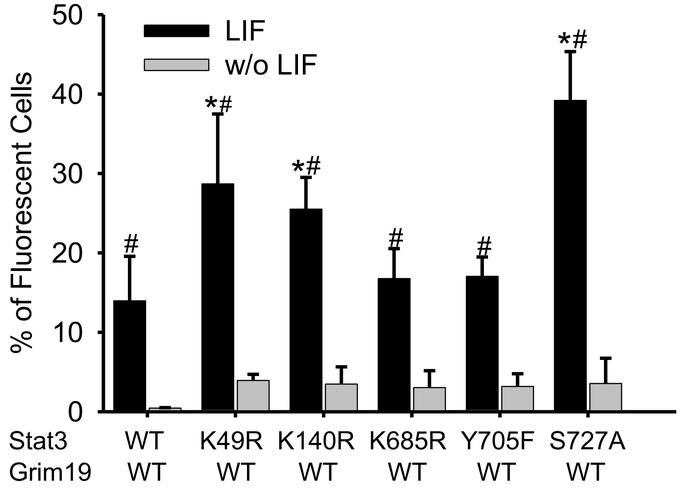
STAT3 Pathways. Non stimulated (1) and stimulated (4) STAT3 homodimers can go to the nucleus where they bind to DNA and activate the transcription of genes. STAT3 can also form heterodimers with the mitochondrial protein GRIM19 (6).



A bimolecular fluorescence complementation (BiFC) assay for the visualization of STAT3 interactions in living cells. STAT3 proteins were fused to two non-fluorescent fragments of the Venus reporter protein. When STAT3 dimerizes/oligomerizes, the two Venus fragments get together and reconstitute the functional fluorophore.



STAT3-GRIM19 heterodimers localize to the mitochondria. HeLa cells were transfected with the V1-STAT3 WT and V2-GRIM19 BiFC constructs. In red, mitochondria stained with Mitotracker dye; in blue, nuclei stained with Hoechst 33342 dye; and in green, STAT3-GRIM19 dimers (Venus fluorescence). STAT3-GRIM19 heterodimers mainly localize to the mitochondria. Scale bar - 20µm



K49, K140 and S727 residues control the interaction between STAT3 and GRIM19 after stimulation with Leukemia Inhibitory Factor (LIF). LIF stimulation increases STAT3-GRIM19 interaction. Mutations that block STAT3 post-translational modifications at K49, K140 and S727 further increase STAT3-GRIM19 interaction. *, significant *vs* WT stimulated pair; #, significant *vs* the corresponding unstimulated pair, p<0.005.