Post-translational modifications modulate STAT3 cellular distribution

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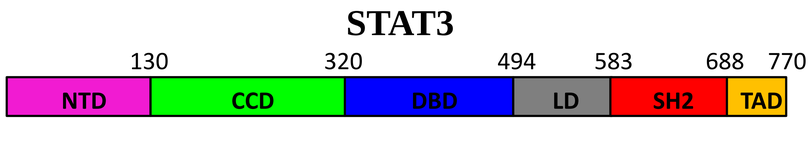
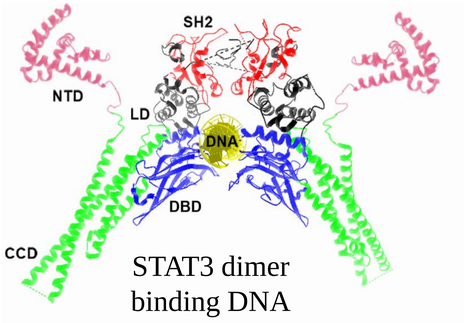
Background





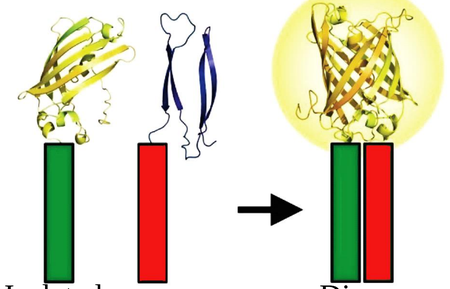
STAT3 dimer binding DNA

- Cytosol, nucleus, mitochondria and endoplasmic reticulum
- Activity regulated by PTMs
- > 80 PTMs sites

Bimolecular Fluorescence Complementation

Venus 1 Venus 2 **Venus 1+Venus 2**

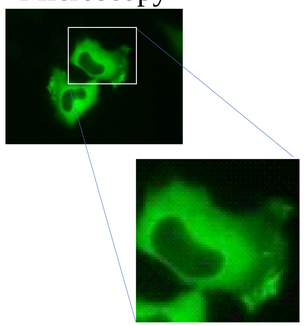
Non-Fluo **FLUO**



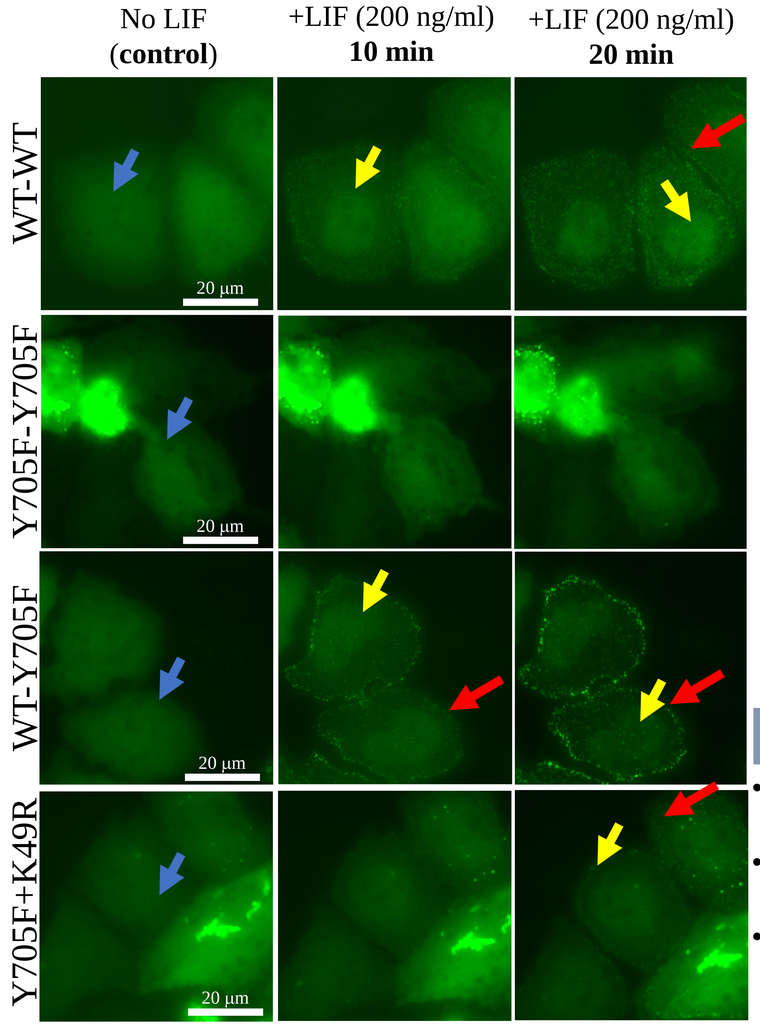
Isolated monomers: Dimer:

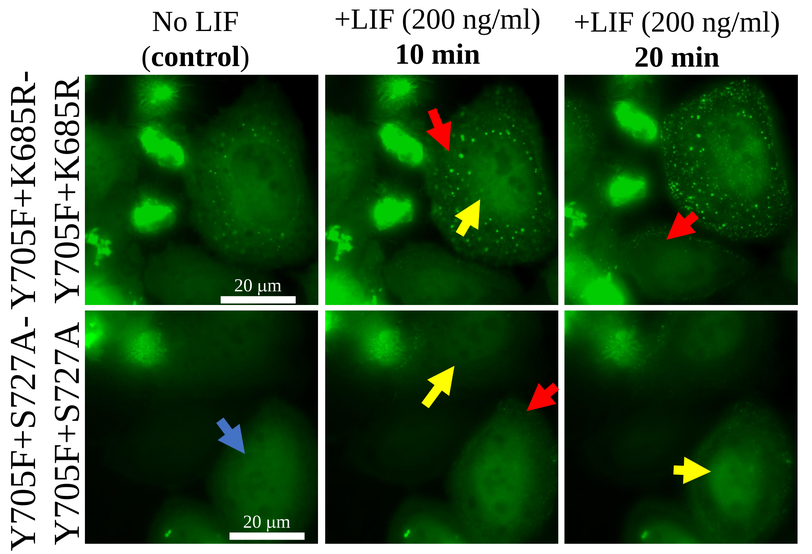
STAT3 STAT3 **STAT3/STAT3**

Microscopy



Time-lapse of STAT3 PTM-inactivating mutants in living HeLa cells (Leica SP8, M: x63)





Blue arrows: Diffuse cytosolic

Yellow arrows: nuclear accumulation

Red arrows: cytosolic punctiform aggregates

Conclusions

- Normal (WT) STAT3 dimers quickly translocate to the nucleus in the presence of the Leukemia Inhibitory Factor (LIF).
- Y705F symmetric pairs prevent LIF-induced nuclear translocation while asymmetric pairs WT-Y705F behave similarly to WT pairs.
- In symmetric pairs, additional mutation to Y705F (double mutant) partially rescues the blocking effect of Y705F single mutant.