Post-translational modifications modulate STAT3 cellular distribution

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Background

- STAT3 contains several domains:
  - NTD: Nuclear Transcription Domain
  - CCD: Cytosolic Core Domain
  - DBD: DNA Binding Domain
  - LD: Lysine (K) Domain
  - SH2: SH2 Domain
  - TAD: Transactivation Domain

- STAT3 is active in the cytosol, nucleus, mitochondria and endoplasmic reticulum.
- Activity regulated by post-translational modifications (PTMs) with >80 PTM sites.

Bimolecular Fluorescence Complementation

- Venus 1: Non-FLUO
- Venus 2: FLUO
- Venus 1 + Venus 2

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

- No LIF (control)
- +LIF (200 ng/ml) for 10 min
- +LIF (200 ng/ml) for 20 min

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.