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Inhibition of Oncogenic functionality of STAT3 Protein by Membrane Anchoring BAOXU LIU, STEVEN FLETCHER, PATRICK GUNNING, CLAUDIU GRADINARU, University of Toronto, GRADINARU/GUNNING COLLABORATION — Signal Transducer and Activator of Transcription 3 (STAT3) protein plays an important role in oncogenic processes. A novel molecular therapeutic approach to inhibit the oncogenic functionality of STAT3 is to design a prenylated small peptide sequence which could sequester STAT3 to the plasma membrane. We have also developed a novel fluorescein derivative label (F-NAc), which is much more photostable compared to the popular fluorescein label FITC. Remarkably, the new dye shows fluorescent properties that are invariant over a wide pH range, which is advantageous for our application. We have shown that F-NAc is suitable for single-molecule measurements and its properties are not affected by ligation to biomolecules. The membrane localization via high-affinity prenylated small-molecule binding agents is studied by encapsulating FNAc-labeled STAT3 and inhibitors within a liposome model cell system. The dynamics of the interaction between the protein and the prenylated ligands is investigated at single molecule level. The efficiency and stability of the STAT3 anchoring in lipid membranes are addressed via quantitative confocal imaging and single-molecule spectroscopy using a custom-built multiparameter fluorescence microscope.

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