Nanoimage Characterization of Fibroblast Growth Factor Receptor 3 Signaling in Bladder Cancer Development

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The overall goal of this research is to characterize the functional consequences of mutations in FGFR3 that have been identified in cancer. Fibroblast growth factor receptors (FGFR) belong to a family of receptor tyrosine kinases (RTK) and are tightly associated with many biological processes, including organ development, cell proliferation and migration. Studies over the past decades have validated the pivotal roles that FGFRs play in tumorigenesis, due to their critical involvement in cell survival, proliferation, inflammation, metastasis and angiogenesis. Using fluorescence fluctuation spectroscopy (FFS) approaches, I have examined stimulus-dependent oligomerization and intracellular trafficking of Halo-tagged FGFR3 in live cells. My research demonstrates that treatment of cells with FGF9 induces dimerization of FGFR3 on the plasma membrane. Therefore, these results validate the use of FFS to characterize the self association of FGFR3 in live cells and provides a quantitative method to study the self-association of bladder cancer mutant forms of FGFR3. The major objective of this research is to determine how disease-linked mutations influence FGFR3 oligomerization on the plasma membrane. I will also test my hypothesis that mutant forms of FGFR3 bypass regulatory processes that normally serve to limit FGFR3 activation and its downstream signaling. This is the first comprehensive study of FGFR3 trafficking in live cells, and is likely to provide important insights into the molecular mechanisms underlying FGFR3-dependent oncogenesis.

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