

Proteomic profiling of the cellular surfaceome reveals new targets for potential theranostic applications in cancers driven by TERT promoter mutations

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Reactivation of telomerase reverse transcriptase (TERT) allows cells to divide aggressively and evade apoptosis. Recent studies have shown that TERT can be an oncogenic driver of virtually all cancer types, including major public health challenges like glioblastoma, bladder cancer, and pancreatic cancer. However, directly inhibiting TERT with small molecule drugs is not feasible. On this basis, we have conducted cell surface proteomics studies to identify proteins upregulated uniquely on the surface of cells with hyperactive TERT. Several proteins have been identified in the human glioblastoma cell line U251. Moreover, we have shown that two proteins, ALCAM/CD166 and ITGAV, are commonly upregulated in several glioblastoma cell lines with TERT promoter mutations. Mechanism studies suggest that the cell surface localization, but not the total protein expression level, of either protein is impacted by the ETS transcription factor complex GABPB1. Because expression of either protein is generally low in normal tissues, we are now working with the Wells lab to apply phage display to generate recombinant human antibodies against these targets. These probes can be easily engineered for theranostic applications to develop one of the first translational strategies to detect or treat cells driven by oncogenic TERT.