Multi-enzyme activated imaging probes for image guided surgery

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Technology description

Stanford researchers at the Bogyo Lab have proposed a method to develop multi-enzyme-activated imaging probes with better selectivity for tumors than current single-reporter probes for fluorescent guided tumor resections. These new probes are dual quenched orthogonal protease substrates, referred to as ‘AND-Gate’ probes and require two independent enzymes (e.g. proteases) that are elevated in tumors to produce a fluorescent signal. Preliminary studies with the probes in a mouse model of breast cancer confirms that the AND-Gate strategy results in higher overall fluorescence intensity at the tumor site while dramatically reducing non-specific activation in healthy tissues compared to single protease targeted probes.

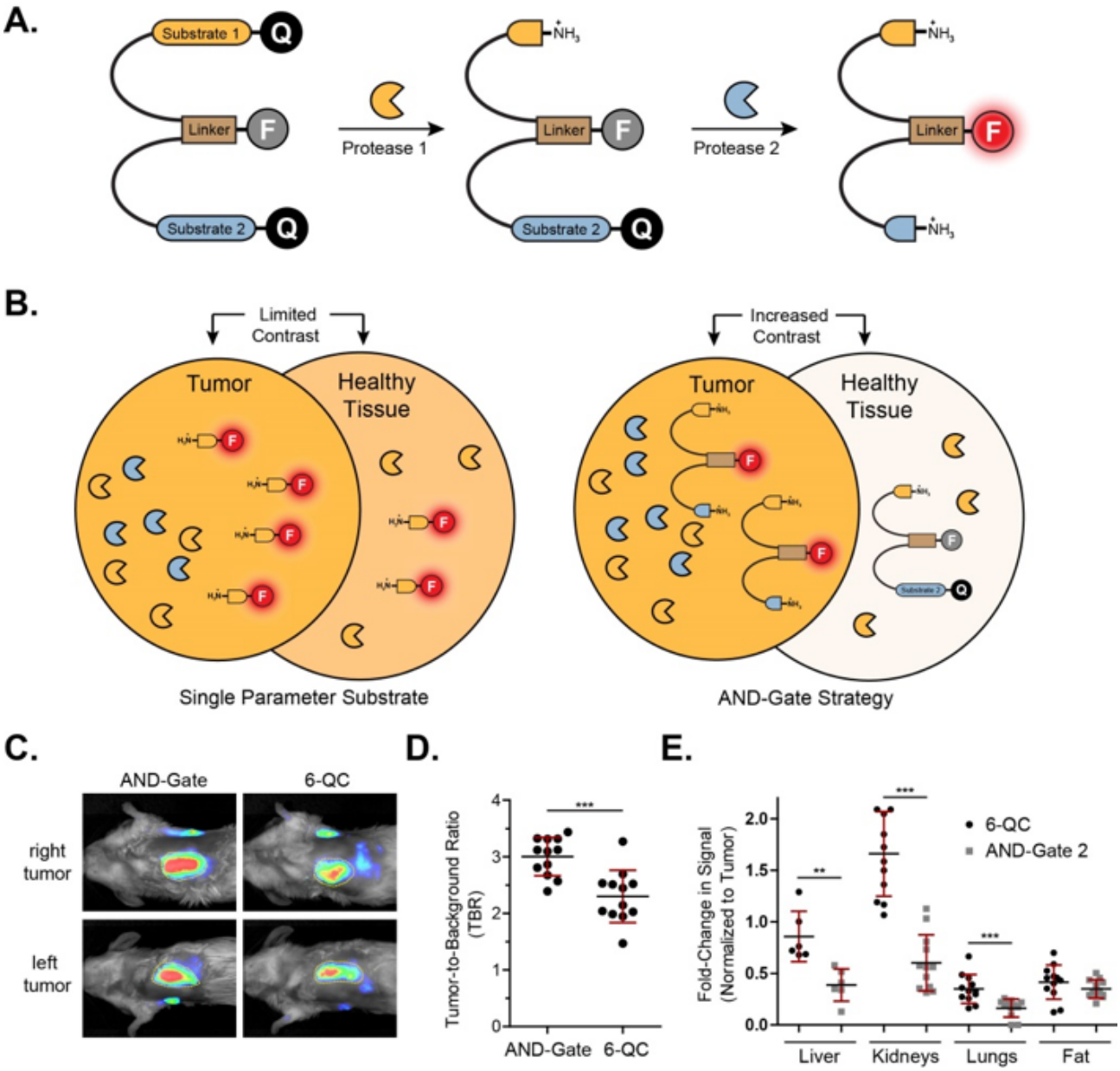

Figure description -A.The ‘AND-Gate’ strategy requires two orthogonal enzymatic processing events to become fluorescently active.B.Single parameter contrast agents have an inherent limit on signal produced in tumors compared to healthy tissues because they rely on expression or activity differences of a single target. The AND-gate approach increases selectivity and contrast between tumors and healthy tissue by requiring a two-step activation of enzymes that are only found in the context of the tumor. Therefore, complete activation only occurs in the tumor microenvironment.C.Our bestAND-Gateprobe and a single substrate probe6-QCwere injected into mice bearing 4T1 breast tumors. TheAND-Gateprobe develops a brighter signal within tumors compared to6-QC, which is a single parameter probe.D.The Tumor-to-Background Ratio (TBR) is significantly better than6-QCdemonstrating this strategy enhances selectivity for fluorescent activation in 4T1 breast tumors (T-test, ***p < 0.001).E.TheAND-Gateprobe significantly reduces signal in healthy organs compared to6-QCincluding the lungs, liver, and kidneys where high background with single substrate probes is common (Student’ s T-test, Benforroni-Holm Procedure: **p < 0.01, ***p < 0.001). This indicates that

the AND-Gate strategy could enhance fluorescent contrast and specificity in tumors compared to current technology in areas containing high background signal.

Institution

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