Personalized Protease fingerprinting for early cancer diagnosis

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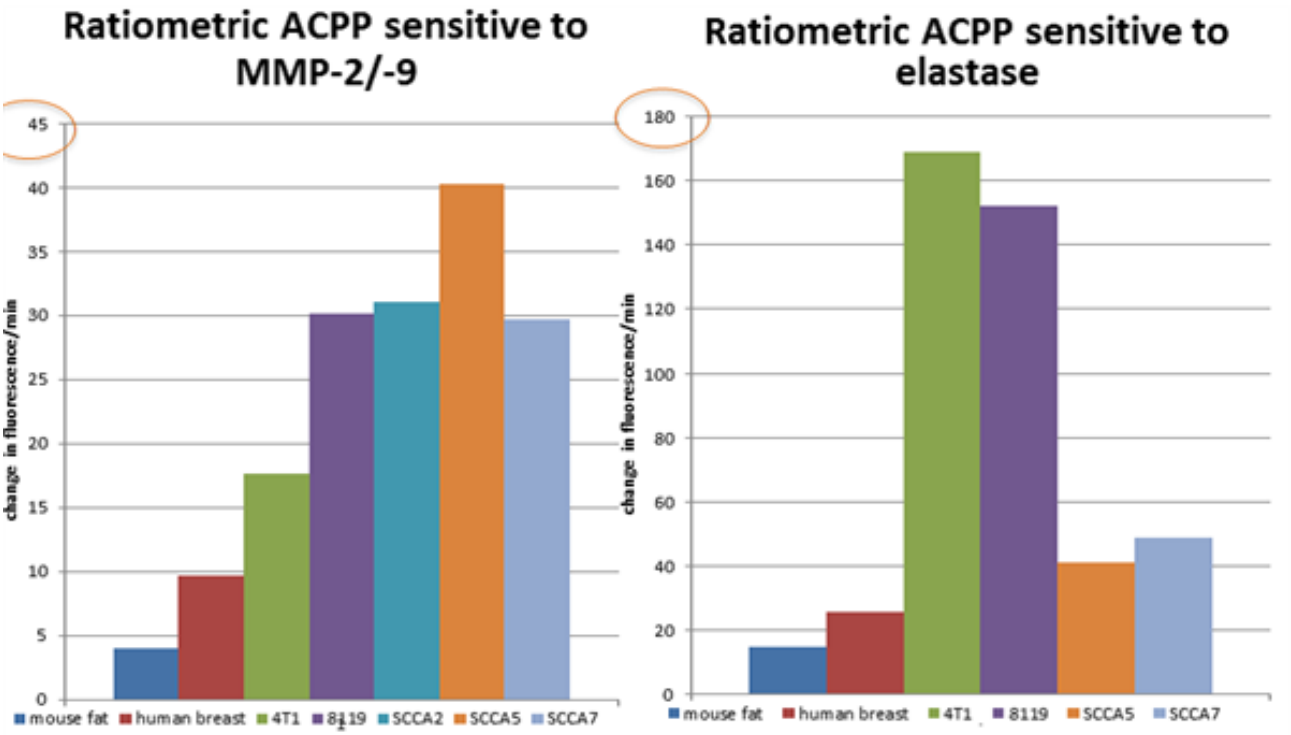
Technology description

UCSD researchers have developed a personalized protease fingerprinting assay which can be useful for improved imaging during surgery and post-surgical assessment of the tumor tissue. The ex vivo assay is based on cleavage of dual fluorescently labeled substrates; the tumor extract' s enzymes cleaves the fluorescent probe, resulting in a personalized profile of the proteases active in that specific tumor. As a proof of concept, the inventors have synthesized the first generation of MMP cleavable probes which have been tested on various (frozen) human tumor samples (breast, head and neck tumors). The resulting protease expression profiles, should make it possible to select the specific probe(s) which can be used for intra-operative imaging and tumor boundary determination. Synthesis of probes for other cancer associated MMPs and non-MMP proteases is underway. The investigators hope to conduct a clinical trial to exploring the correlation of protease activity with several clinically relevant parameters.

Sample Data

(change in fluoresence/min)



Key: 4T1 and 8119 represent mouse breast cancer grafts
SCCA2, SCCA5 and SCCA7 represent human head and neck squamous cell carcinomas
Matrix metalloproteinases (MMPs) as well as other proteases play a crucial role in cancer invasion and metastasis. Increase in MMP levels correlate with higher stage, increased cancer grade and higher activity when overexpressed in malignant tumors and is associated with poorer patient prognosis. The expression of proteases in clinical tumors has been studied through measurement of mRNA levels and immunoassays. These techniques monitor the sum of all forms of the protease, much of which is either inactive proenzyme or inactive complexes that have endogenous inhibitor proteins (e.g. TIMPs). Recent methods for detection such as "in situ zymography" is slow and qualitative. The ability to accurately measure and/or monitor the active enzyme in a patient's tumor could provide improved intra-operative imaging of tumor margins by utilizing a fluorescent probe which is specific for the tumor's protease(s). Obtaining the expression profile of tissue excised during surgery could aid with the assessment of post-surgical options.

Additional Technologies by these Inventors

Channelrhodopsin Mutants with Improved Channel Kinetics and Other Properties
Molecules for Labeling Peripheral Nerves for use in Image Guided Surgery and Other Clinical Applications
Proteins that Efficiently Generate Singlet Oxygen Background
Proteins That Fluoresce At Infrared Wavelengths Or Singlet Oxygen Upon Illumination
Dual Reflectance-Fluorescence Guided Surgical System

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