Spotlight

By Gina Kirchweger

Matriptase: Seeing Is Believing

Napp *et al*.
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Medical imaging is widely used by oncologists to monitor tumors and their response to treatment regimens. Mostly driven by the advance of new imaging technologies that allow researchers to noninvasively visualize and monitor molecular and cellular processes that play a crucial role in tumorigenesis, imaging has become a powerful tool to develop and validate novel concepts for cancer therapy.

Napp *et al*. made use of one such technology, time-domain near-infrared fluorescence (NIRF), which can deeply penetrate biological tissues and thus allowed them to assess *in vivo* expression and activity of matriptase and evaluate the molecular efficiency of synthetic matriptase inhibitors in an orthotopic mouse model of AsPC-1 pancreatic carcinoma. Matriptase, a trypsin-like epithelial serine protease, is required for global homeostasis of diverse epithelial tissues. However, it is also consistently overexpressed in a variety of epithelial cancers, and even modest overexpression in a transgenic mouse model was sufficient to induce malignant transformation, marking the enzyme as a potential target for a novel cancer therapy.

By applying time-domain NIRF imaging in combination with a Cy5.5-labeled matriptase-specific antibody, the authors could demonstrate *in vivo* matriptase expression in primary AsPC-1 tumors as well as tumor nodules on scars and in distant metastases. They confirmed their results by *ex vivo* NIRF imaging of the respective organs and by fusing the *in vivo* acquired 2D-NIRF intensity maps with high-resolution 3D-CT data sets obtained through flat-panel volume computed tomography (fpCVT) of living mice. Further experiments with synthetic active-site inhibitors support the notion of matriptase as a promising molecular target for the development of inhibitor-based cancer treatments.

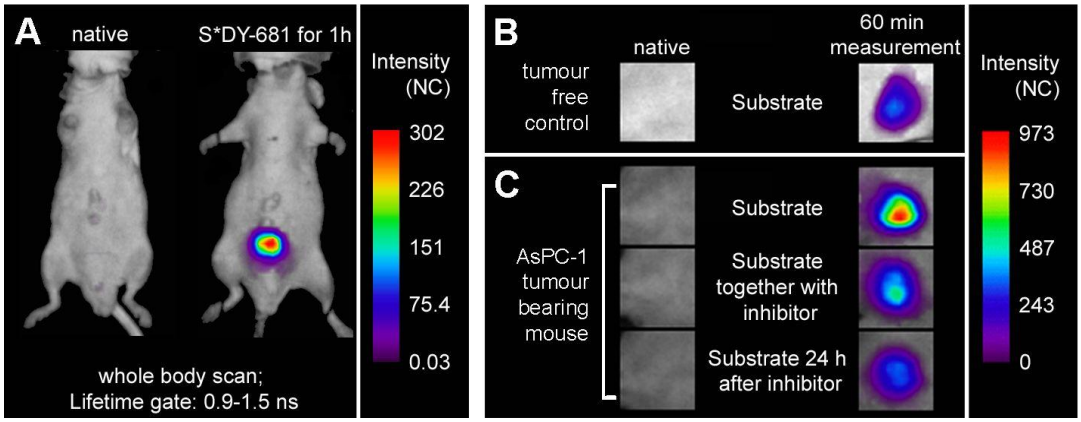

Figure 8: Matriptase activity and its inhibition in vivo in the orthotopic AsPC-1 tumor model. (A) Representative whole-body scans of an AsPC-1 tumor-bearing mouse taken before (native) and 60 min after i.v. injection of the activatable flourogenic probe S*DY-681. High fluorescence intensity was measured only over the bladder area, where the cleaved substrate accumulated after renal excretion. (B,C) Representative eO scans taken over the bladder area before and 60 min after i.v. injection of S*DY-681. Flourescence intensities increased upon cleavage of S*DY-681 by matriptase in (C, upper panel) tumor-bearing mice. Matriptase activity was blocked for at least 24 h by application of CU-1737 inhibitor to the same mouse as indicated by lower fluorescence intensities in measurements performed immediately and 24 h after application of the inhibitor.