Spotlight

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MMP11 and Metastasis: A Complicated Relationship

Brasse *et al*.
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Ever since the importance of matrix metalloproteinases (MMPs) in cancer progression was discovered, they have been regarded as major critical molecules assisting tumor cells during metastasis. But over time, as evidence emerged that members of the MMP family can exhibit pro-metastatic as well as anti-metastatic roles—depending on their nature and the experimental setting, a more nuanced view began to take hold.

The latest study by Brasse *et al*. emphasizes the complexity of the metastatic process, in which the same factor—in this particular case MMP11, also known as stromelysin-3—can take on activator or repressor function, depending on the metastatic step. The authors injected C26 colon cancer cells into either wild-type or MMP11-deficient mice and monitored metastasis via microCT, a highly sensitive technique which allows real-time imaging of developing metastases in living mice. They found that it took longer for lung metastases to become established in the absence of MMP11 and they were smaller in volume than those in control mice. However, and paradoxically, the total number of lung metastases was 2-to 3-fold higher in MMP11-deficient mice, suggesting that MMP11 might limit the spread of cancer. Indeed, the second step of metastatic development, the colonization of other organs, was more efficient in MMP11-deficient mice.

The complex spatio-temporal relationship between cancer spread and MMPs may partly explain why the first generation of broad-spectrum MMP inhibitors failed in the clinic. A better understanding of MMPs' role in the interaction between tumor cells and stromal cells should allow the determination of specific windows in cancer treatment when specific MMP inhibition could have a valuable therapeutic effect.

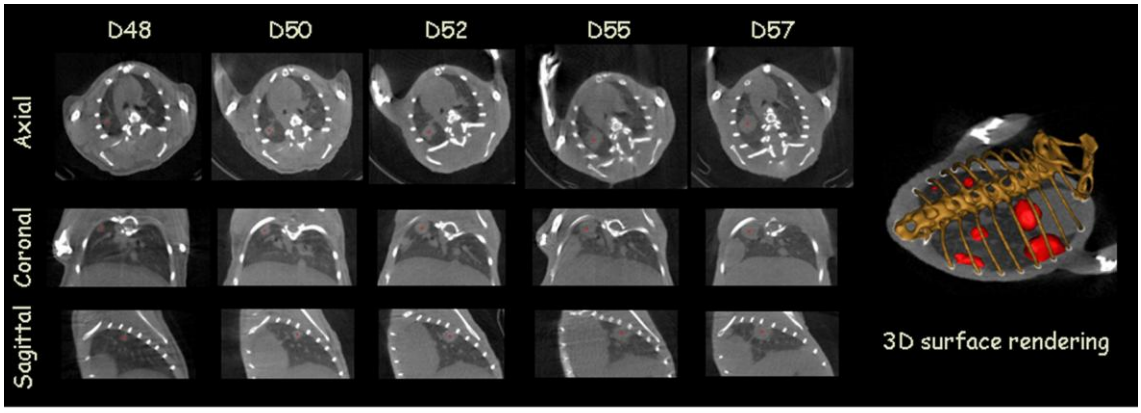

Figure 1
Brasse et al.

Figure 1: Kinetics of lung metastasis in live mice using microCT imaging. Axial, coronal and sagittal virtual sections in the lung of one MMP11-deficient mouse were used to follow the occurrence and growth of several lung metastases between day 48 and 57.