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Leading technology for in vivo fluorescent sarcoma imaging

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Background: Naturally fluorescent proteins have revolutionized biology by enabling what was formerly invisible to be seen clearly. The green fluorescent protein (GFP) gene is frequently used as a reporter of expression and a biosensor in living animals. However, in orthopedic research, fluorescent proteins have only been used in a limited fashion. We have developed fluorescent real-time imaging for sarcoma cells by means of multi-color fluorescent cell lines and transgenic mice. Methods:
Sarcoma cells were labeled with GFP or red fluorescent protein (RFP). Color-coded cells were transplanted into bone, spinal cord, or lung and their dynamics were observed in live mice. Transgenic mice were also used as the host in which GFP was driven by a stem cell marker nestin. Nascent blood vessels and immature neurons expressed GFP in this model. Indocyanine green was injected into tumor bearing mice to visualize tumor mass and peritumoral vascular structure. Results:
Fluorescence imaging readily distinguished the color-coded cell lines and their differential ability to survive at the primary sites as well as metastasizing in live mice. Imaging of sarcoma cell trafficking in vessels revealed critical steps of metastasis. In transgenic mice, nascent blood vessels in the growing tumors were visualized. Lung metastasis was observed directly under fluorescent light and a large number of cells were arrested but the cell number decreased rapidly at 24 hours. Single disseminated cells tended to die earlier than cells in aggregates. Dual colored fibrosarcoma cells were also injected into either the portal vein or abdominal aorta in nude mice. The liver and muscle were imaged to visualize the fate of the cells. The rate of sarcoma cell death was highest in the lung and lowest in the muscle. In each organ, single disseminated cells tended to die earlier than aggregated cells. Indocyanine green can image tumor angiogenesis and peritumoral lymphatic channels. This technology can be utilized fluorescent guided surgery, such as tumor imaging, avoiding vascular injuries and sentinel lymph node biopsy. Conclusion:
Real time in vivo imaging of sarcoma cells enabled visualization of their dynamics, including cell mobility, invasion, metastasis and angiogenesis.

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