Biology and Pathology

Cancer Biology

Imaging Tumor Hallmarks
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Learning Objectives:

- Know the hallmarks of cancer and their related sequelae
- Identify approaches to image these parameters with molecular imaging
- Describe the clinico-biological significance that such imaging can provide

There is considerable inter- and intra- tumoral genetic heterogeneity, which is a challenge for molecularly targeted therapy. In contrast, virtually all cancers exhibit common phenotypic traits, or "Hallmarks". These hallmarks are not only useful to monitor the response to canti-cancer therapies, they are also being considered as therapeutic targets themselves. These traits, such as resistance to apoptosis, growth factor independence, altered bioenergetics, angiogenesis and invasion, call all be understood as adaptive strategies to the microenvironmental landscape that is temporally changing during the course of cancer progression. Also important is that many of these traits are imageable through molecular imaging approaches, using optical, PET and MR. In this talk, we will review the hallmarks of cancer and discuss approaches that can be used to assess their activities through molecular imaging. Over past decade there has been a significant effort to expand the armamentarium of available imaging biomarkers to those that are more sensitive to tumor metabolism, molecular expression or physiology, and following are a few examples. Some of these are directed specifically at a hallmark, such as FDG PET, which reports on altered bioenergetics, or integrin-targeted agents, which report on angiogenesis. Other approaches are more indirect, such as diffusion MRI, which reports on cellularity, perfusion imaging which reports on dysregulated vasculogenesis, and pH imaging, which is a sequela of altered bioenergetics. Hypoxia is also emerging as a common microenvironmental hallmark of cancer, and there are numerous molecular imaging approaches to visualize this parameter. In some cases, expression of a hallmark results in the altered expression of cell surface antigens, and tracers can be directed at these to interrogate, for example, cell proliferation or apoptosis/necrosis.

Relevant Publications:

1. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 144(5):646-74, 2011
2. Gillies RJ, Verduzco D, Gatenby RA. Evolutionary dynamics of carcinogenesis and why targeted therapy does not work. Nature reviews Cancer 12:487-93, 2012
3. Nowell PC. The clonal evolution of tumor cell populations. Science (New York, NY 1976;194(4260):23-8.
4. Gerlinger M, Swanton C. How Darwinian models inform therapeutic failure initiated by clonal heterogeneity in cancer medicine. British journal of cancer 2010;103(8):1139-43.
5. Gerlinger M, Rowan AJ, Horswell S, et al. Intratumor heterogeneity and branched evolution revealed by multiregion sequencing. The New England journal of medicine 2012;366(10):883-92.
6. Gatenby RA, Gillies RJ. A microenvironmental model of carcinogenesis. Nature reviews 2008;8(1):56-61.
7. Gatenby RA, Gillies RJ. Why do cancers have high aerobic glycolysis? Nature reviews 2004;4(11):891-9.