

Specialty area: Molecular & Cellular Imaging: From the Bench to the Bed

Agent Synthesis and Functionalization: From Small Molecules to Nanoparticles

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Target audience: investigators and trainees with interests in chemistry and preparation of molecular and cellular imaging agents;

Highlights:

- Choosing right chemistry and approaches to make small molecule or nanoparticle agents for cellular and molecular imaging applications;
- Using specific surface coating materials or carriers for modifying the stability, biodistribution and biocompatibility of the agents;
- Improving contrast effects through modifications of surface coating;
- Functionalizing agents with targeting ligands for cell specific targeting;

Cellular and molecular imaging applications require the high sensitivity and specificity in order to visualize biological and disease processes at molecular and cellular levels. The molecular and cellular imaging agents, or probes, often need to have several folds or orders of magnitude higher contrast effect than that of clinically used MRI contrast agents. There is a range of synthetic and chemical preparation approaches that have been developed to make molecular and cellular agents based on small molecule gadolinium chelators and magnetic nanoparticles, such as iron oxide nanoparticles. Because MRI based molecular and cellular imaging agents are used in living systems, agents need to be water soluble, highly stable, and biocompatible in the biological environment. To obtain these properties, chemical modifications with synthetic polymers or other macromolecules can be used not only to solubilize nanoparticle agents in the aqueous medium and physiological condition but also stabilize the agents from aggregations and precipitations. Furthermore, surface coating and modification can alter and facilitate the interaction between exogenous contrast agents and biological systems to improve the cell penetration and internalization, biodistributions, clearance and pharmacokinetics of the contrast agents in order to enhance the delivery and accumulations of the agents in specific cells, tissue and organs of interest. Surface modifications can also be used to reduce non-specific off-target accumulation of the agents. For biomarker targeted imaging agents, contrast agents can be further functionalized by chemically conjugating or linking specific ligands, such as an antibody, peptide or an antibody fragment, small peptide, oligonucleotide. This lecture will give a brief overview of several common chemical methods used for synthesis of small molecule molecular imaging probes and magnetic nanoparticles to achieve high relaxivities and contrast effects for high sensitivity MRI detection, which are highly dependent on chemical structure, composition and size of the agents. The strategies for making and selecting surface coating materials or carriers for modifying the stability, biodistribution and biocompatibility of agents, as well as improving MRI contrast effects by changing and modifying coating materials, will be discussed. In addition, several examples will be presented to demonstrate the approaches and chemistry that can be applied for conjugating biomarker targeting ligands and moieties to functionalize contrast agents, particularly nanoparticles, for targeted imaging and cell labeling.