

selective, but have a high propensity to undergo non-selective binding to plasma proteins such as albumin can present a significant challenge in an imaging experiment. Non-specific binding of the radioligand can substantially decrease the signal to noise ratio in a PET/SPECT imaging experiment. The radioligand would certainly bind to the intended biomolecular target and generate an observable signal, but it would also produce an observable signal in every non-specific binding event that it takes part in. If this non-specific binding is to albumin, then the radioligand would be nearly omnipresent in the body, as albumin is a major component of plasma. This could potentially drown out the signal from the macromolecule of interest. Expression levels of the biomolecular target also play a role in the signal to noise ratio in a PET/SPECT imaging experiment. Higher expression levels of the target macromolecule typically lead to better signal quality, while biomolecules with lower expression levels are more difficult to visualize.

The PK properties necessary for a successful radioligand are also not the same as those associated with therapeutic agents. Rapid uptake is highly desirable, especially in PET imaging agents where radioactive decay is rapid. In addition, a short pharmacokinetic half-life would decrease risk to subjects as a result of decreased exposure time to radioactive material. Pgp efflux can also be a substantial issue in the development and use of a radioligand. This is especially true if the targeted macromolecule is in the brain, as Pgp is heavily expressed in the blood–brain barrier. Finally, translation of the target between species should be high (e.g., the radioligand can be used to visualize the biomolecular target in animal models and humans). A radioligand that is useful in rats and dogs, but not in humans may provide some interesting information about the animal model, but it will be of limited predictive value in the human condition.

Magnetic resonance imaging (MRI) is an alternative technique that is also routinely employed to obtain detailed images of a subject. As the name implies, this imaging method is based on nuclear magnetic resonance techniques that are commonly employed in the study of organic and organometallic compounds. This method takes advantage of differential responses of hydrogen atoms to radio frequencies when they are in a magnetic field (other atoms can also be observed using this technique, but this discussion will be limited to hydrogen atoms). In brief, hydrogen atoms absorb energy when they are irradiated in the radio frequency range (60–1000 MHz) and move to an excited state. When the hydrogen atom relaxes back to the ground state, it releases energy that can be detected. The specific resonance frequency of any given hydrogen atom is dependent upon the nature of its immediate environment at the molecular level, and as a result, even small difference between two different hydrogen atoms can be detected and quantified. At the macroscopic level, differences in hydrogen atoms in various areas of the body can be mapped using sophisticated instrumentation designed to subject the body to a