8.5.1 ^{11}C AND ^{18}F

The short-lived positron emitting radionuclides that have had the greatest impact in PET are ^{11}C and ^{18}F. Carbon is a ubiquitous building block of life, and the most abundant isotope of carbon (^{12}C) can be substituted for ^{11}C without influencing the bioactivity of the molecule. Thus, the number of ligands that could be ^{11}C-labeled is in principle unlimited. Fluorine containing compounds are not abundant in nature, but popular in drug discovery due to its ability to engage in hydrogen bonding and influence the metabolic rate of compounds. Nevertheless, known ligands may often have to be modified and re-evaluated before an ^{18}F-moiety can be introduced and the ligand be applied to PET studies.

The short half-life of ^{11}C is both an advantage and a challenge. Chemical modifications have to be conducted as fast as possible. A rule of thumb suggests that a radioactive synthesis should not exceed 2–3 half-lives which in the case of ^{11}C provides 1 hour for all the necessary manipulations. Thus, the final application has to be in close proximity to the site of synthesis and the labeled product cannot be transported to other facilities. On the other hand, the half-life is long enough to investigate many biological processes like drug–receptor interactions. In addition, test–retest experiments are feasible in 1 day using the same animal.

^{18}F has a significant longer half-life (110 minutes) than ^{11}C (20 minutes), providing additional time to perform more complex synthetic manipulations and biological experiments with the final PET ligand. Additionally, it is possible to synthesize the radioligand at one facility and subsequently transport it to another site. ^{18}F possesses a relatively low positron energy resulting in a mean β^+-range of 0.6 mm in water, which leads to PET images with high spatial resolution in combination with a relatively low radiation burden for the patient. All of these factors taken together means that ^{18}F is very useful and very widely applied in PET.

8.5.2 ^{68}Ga, ^{64}Cu, AND ^{89}Zr

In contrast to ^{11}C and ^{18}F, which typically are covalently linked to the PET ligand, metal nuclides rely on chelating groups that have to be attached to the target molecule. These entities bind a single metal ion by two or more separate coordinate bonds (see Figure 8.4 for an example). The coupling of the chelator to the original ligand obviously influences the pharmacodynamic and pharmacokinetic behavior and ultimately, changes the affinity, selectivity, biodistribution and metabolism of the compound, but in some cases, these changes are tolerated. ^{68}Ga-DOTA-Tyr3-octreotide, a somatostatin analog targeting neuroendocrine tumors, is a good example of a metal-based tracer, see Figure 8.4.

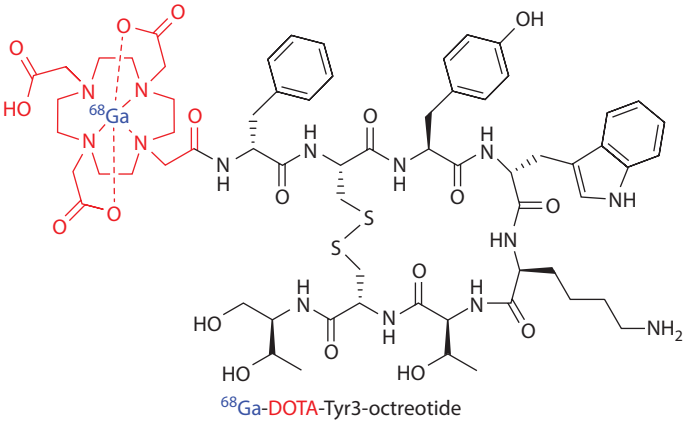

FIGURE 8.4 Example of ^{68}Ga-PET ligand. The DOTA-chelator (in red) is appended to the active peptide (in black) without disturbing its ability to interact with the desired target. The PET ligand is synthesized simply by adding a solution of $^{68}Ga^{3+}$ to the peptide-DOTA precursor.