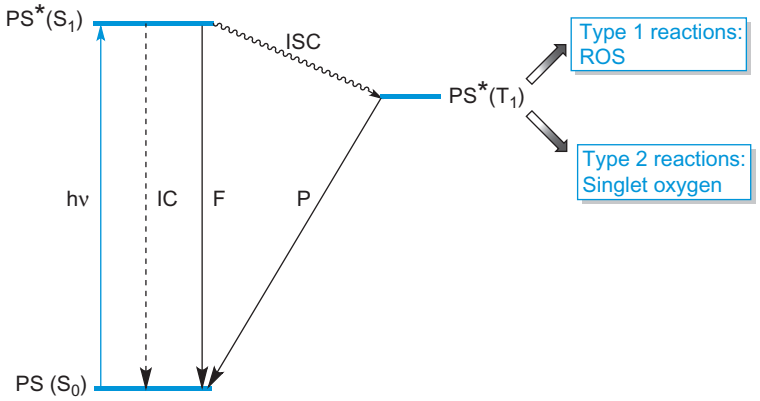

FIGURE 4.52

Jablonski diagram illustrating schematically the electronic transitions involved in photodynamic therapy.

The following are the main requirements that the ideal photosensitizer in cancer photodynamic therapy should satisfy:

1. Selectivity to tumor cells.
2. Biological stability, with no cytotoxicity in the absence of light.
3. Photostability—that is, low sensitivity to oxidation by singlet oxygen.
4. Strong absorption in the 600- to 800-nm region of the spectrum (red to near infrared).
5. Photochemical efficiency and long triplet excited state lifetime.
6. Good tissue penetration. This is better achieved if the absorption maximum is in the near-infrared (NIR) region, where tissue absorption is minimal. Thus, a tissue penetration depth of 4 mm can be obtained using a 763-nm light source, whereas a 630-nm radiation, corresponding to the absorption maximum of a typical porphyrin, has only 1.6-mm penetration.[135]

As shown in Figure 4.53, there are four main stages in the treatment of cancer by photodynamic therapy:

1. Delivery of the photosensitizer, which, with the exception of skin cancers, is normally done by intravenous injection (vascular targeted photodynamic therapy).
2. Ideally, the photosensitizer should be accumulated in the tumor. The lack of such selective accumulation of photoactivable molecules within tumor tissues is the main potential problem of PDT, and for this reason the development of targeted photosensitizers is an active research area.[136]
3. Approximately 24–72 hours after injection, selective irradiation of the target tissue is performed. This is normally achieved by use of a fiber-optic diffuser inserted through an endoscope, which leads to local activation and the generation of singlet oxygen and ROS.
4. Selective tumor destruction by these highly reactive species. Due to the low stability of the toxic species involved, diffusion to surrounding healthy tissues is not significant, and therefore the method is minimally invasive and is well tolerated. In addition to the direct killing of cancer cells, PDT can damage blood vessels in the tumor, preventing the access of necessary nutrients. It also may activate the immune system to attack the tumor cells.[137]