associated with the malignant transformation. Among different approaches that make use of the self-assembly, the biocatalytic self-assembly (BSA) concept has emerged as a new approach in cancer research and is the focus of this chapter. BSA makes use of an enzyme sensitive moiety (group or bond) that is incorporated in a peptide amphiphile (PA) to prevent the PA self-assembly. This moiety is transformed (e.g., cleaved) under the action of the respective enzyme typically resulting in a rebalancing of the amphiphilicity of the PA. As a result, the obtained molecules are able to self-assemble into nanofibers that can further generate two-dimensional networks or localized supramolecular gels under physiological conditions (Yang et al. 2004; Ulijn 2006; Gao et al. 2009; Hirst et al. 2010). This concept, and the fact that cancers present an overexpression of different enzymes, led to the development of BSA approach as: a cancer diagnostic and imaging methodology; a direct anti-cancer strategy (due to the cytotoxicity of the nanofibers themselves or their network); and to induce the controlled release of drugs or pro-drugs. All these strategies will be discussed in the following sections.

Self-Assembling Hydrogels for the Diagnosis of Cancer

Malignant transformation and tumour metastasis are associated with altered expression of a number of biomolecules, such as proteins and glycans. Some of these biomolecules have been identified and nowadays are used as hallmarks for certain cancers, aiding the staging, monitoring and prognosis (invasion and metastasis) of these diseases. Many others remain to be discovered. Thus, the development of molecular tools for selective detection of these biomarkers is of fundamental importance for both basic cancer research and cancer diagnosis. Approaches, involving different fluorescent probes together with non-invasive methods for their detection (e.g., endoscopic molecular imaging), are quite attractive as they can avoid unnecessary biopsies. Moreover, they are cost effective and allow real time observation. The main challenge in these approaches is the design of a probe that is sufficiently selective (cancer cells share many common features with the normal host cells from which they derive) and sensitive (easily distinguished from the background signal). During the last five years, supramolecular self-assembly of small molecules has been applied in several strategies for design of fluorescent probes that meet such criteria. These probes are typically composed of a core self-assembling unit—such as a short PA derivative of diphenylalanine (Fig. 1, blue), and a biologically sensitive unit (functional group or bond, Fig. 1, green). The amphiphile capping groups are polycyclic aromatic hydrocarbons (R in Fig. 1), which not only provide driving force for the self-assembly via aromatic interactions (π-π interactions) but also endows the obtained supramolecular structure with intrinsic fluorescent signal. Depending on the chosen approach, the design of the probe can include additional fluorescent units (e.g., 4 in Fig. 1).

The principle that drives the self-assembly dependent imaging is that the properties of a fluorophore incorporated into the probe-gelator are quite different if the molecules bearing them are assembled or not. Characteristic shifts are observed for different molecular organisations: hypsochromic shift (blue shift) is typical for the H-assemblies, in which the transition moments of the monomers are organized in a "face-to-face" manner, i.e., aligned parallel but perpendicular to the line joining their centres. In