Application of synthetic biology to the development of smart therapeutic nanosystems against cancer

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Abstract

Our understanding of the molecular and cellular basis of cancer has improved considerably over the past few decades. However, this has not been paralleled by proportional increases in long-term survival rates of patients affected by the disease, which still remains the second leading cause of death in Europe and North America.

Pharmacological treatment of cancer requires potent inducers of cell death that are also very selective. Classical chemotherapeutic agents are very effective at killing cells but display poor selectivity, leading to excessive collateral damage and limiting their efficacy and clinical application. Molecularly targeted drugs, developed with the advent of functional genomics and high throughput technologies, are more selective than classical chemotherapeutic agents. However, too frequently these compounds do not induce significant cancer cell killing, which also has negative implications for therapeutic outcomes.

Innovative approaches are required to treat cancer effectively. Ideally, these therapeutic strategies should display killing efficiencies similar to those observed with classical chemotherapeutic agents, and target selectivities like those featured by molecularly targeted drugs. Synthetic biology is an emerging field of research that applies engineering principles to the design and construction of artificial biological systems capable of executing pre-determined functions with great control and precision. Following this approach, our laboratory has produced synthetic systems capable of distinguishing cancerous cells from normal cells, and of exploiting cancer biomarkers to promote the suicide of tumor cells whilst conferring active protection to normal cells to avoid off-target cytotoxicity. These systems, their performance, future potential and limitations will be presented and discussed.