SYNTHETIC DESIGN OF A THERAPEUTIC BACTERIUM: DENSITY-DEPENDENT INVASION OF CANCER CELLS

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ABSTRACT

Bacteria are known to localize to tumors after intravenous injection. Based on this phenomenon, therapeutic strains have been developed that attack tumor cells, elicit an immune response, or deliver a therapeutic agent. These strains are often based on attenuated pathogens and display toxicity in humans.

Starting with non-pathogenic E. coli as a chassis, we have engineered a strain that can attack malignant cells by linking genetic modules from heterologous species. To induce cellular invasion at high densities of bacteria, a gene from Yersinia pseudotuberculosis is placed under the control of the quorum sensing system from Vibrio fischeri. This bacterium is able to invade cultured human cancer cells under conditions of high bacterial cell density, conditions known to occur selectively in the tumor microenvironment. This strain represents a platform onto which modules can be added that confer specific adhesion to host cells and program the release of a therapeutic agent.

Advantages of the technology:

? Non-toxic, specific targeting of malignant tumors

? Virulent only in the tumor environment

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