Dokumenttyp: journal article

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Titel des Beitrags: Engineering of bacteria for the visualization of targeted delivery of a cytolytic anticancer agent.

Abstract: A number of recent reports have demonstrated that attenuated Salmonella typhimurium are capable of targeting both primary and metastatic tumors. The use of bacteria as a vehicle for the delivery of anticancer drugs requires a mechanism that precisely regulates and visualizes gene expression to ensure the appropriate timing and location of drug production. To integrate these functions into bacteria, we used a repressor-regulated tetracycline efflux system, in which the expression of a therapeutic gene and an imaging reporter gene were controlled by divergent promoters (tetAP and tetRP) in response to extracellular tetracycline. Attenuated S. typhimurium was transformed with the expression plasmids encoding cytolysin A, a therapeutic gene, and renilla luciferase variant 8, an imaging reporter gene, and administered intravenously to tumor-bearing mice. The engineered Salmonella successfully localized to tumor tissue and gene expression was dependent on the concentration of inducer, indicating the feasibility of peripheral control of bacterial gene expression. The bioluminescence signal permitted the localization of gene expression from the bacteria. The engineered bacteria significantly suppressed both primary and metastatic tumors and
prolonged survival in mice. Therefore, engineered bacteria that carry a therapeutic and an imaging reporter gene for targeted anticancer therapy can be designed as a theranostic agent.