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Effectiveness of therapeutic Salmonella Typhimurium in selectively targeting human cancer cell lines

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Studies indicate that non-virulent strains of Salmonella Typhimurium have tumor-targeting activity. Indeed, S. Typhimurium has been observed to selectively target cancer tissue by a ratio of over 1000:1. Most of these studies focused on the cancer cell selectivity of one strain, the genetically modified S. typhimurium VNP20009. One such study found that a single IV injection of VNP20009 produced tumor growth inhibition of 57 - 95% in mice. Another study conducted by Thamm and associates found that administration of VNP20009 results in dectable bacterial colonization of tumor tissue and partial anti-tumor activity in tumor-bearing dogs. Despite its selectivity, VNP20009 was shown to be too toxic when given to patients in phase I clinical tests. Scientists at Columbia's Cancer Research Center developed a therapeutic strain, CRC2636, an archival strain of S. typhimurium that has been shown to destroy PC-3M without extensive lysis of the cancer cells, a factor thought to contribute to the toxicity of VNP20009. Our research strategy involved analyzing the effectiveness of CRC2636 in selectively targeting prostate, breast, and colon cancer cell lines when incubated with their normal counterparts. In order to track CRC2636 in the attachment and invasion studies, we electroporated pRST plasmids that constitutively expressed the fluorescent mCherry protein into our therapeutic strain. Attachment studies were done on a time course from 10 minutes up to 4 hours and invasion studies were done up to 16 hours. Quantitative results were obtained by counting the number of attached bacterial cells to the cancerous and normal cells at the various time points tested.