Cancer Targeting Activity of Salmonella Invasion Protein A (SipA)

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Due to the fact that current conventional cancer treatments, such as chemotherapy and radiation therapy, lack specificity, the development of new forms of therapy is essential to decreasing negative impacts of the treatment on patients. Past research shows that Salmonella typhimuriuim is able to affect metastases and also preferentially colonize in mouse tumors 2000-fold more than in liver, spleen, lung, heart, and skin. Although, there has been extensive research on chemical compounds that attract the bacteria to tumors, the precise mechanisms of the attractive interaction between bacteria and cancer cells are still unknown. Salmonella Invasion Protein A (SipA), known to change actin filament activity in the host cell, was tested for its potential role in cancer specific delivery of toxic proteins. In this research, a DNA restriction endonuclease (RE) fused with nuclear localization sequences (RE-NLS) was used. The NLS was hypothesized to take the RE-NLS fusion protein to the nucleus of the cancer cells, where the restriction enzyme would cut the cancer cell's genomic DNA and kill the cell. SipA and RE-NLS proteins were mixed with a protein transfection agent to initiate intracellular delivery of the proteins into normal and lung cancer cells from humans and mice. Toxicity assays of the proteins showed a decrease in the number of cancer cells in a dose-dependent manner, while the number of normal cells stayed relatively consistent. Tests using different combinations of SipA and RE-NLS showed greatest decrease in the number of cancer cells when SipA and RE-NLS were given together. Thus, this study gives positive evidence that the SipA protein could potentially be a useful mediator for cancer specific drug delivery in the future.