

# *In vivo* antigen delivery by a *Salmonella* type III secretion system for therapeutic cancer vaccine development

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Bacterial vectors offer many advantages over other antigen delivery systems for the construction of cancer vaccines because they are usually endowed with the ability to potently stimulate the innate immune system (1). This is particularly the case for *Salmonella typhimurium*, which has been extensively used as an antigen delivery vector to construct vaccines against various infectious diseases (2). We have recently developed a system that significantly improves the utility of *Salmonella* as an antigen delivery vehicle (3, 4). This system is based on the use of a specialized protein secretion apparatus (termed type III) that is normally utilized by *Salmonella* to deliver effector bacterial proteins into the extracellular medium as well as into the cytosol of infected cells (5). We have adapted this system to deliver heterologous proteins into class I- and class-II antigen presenting compartments and found that antigens delivered by this system stimulate strong immune responses both *in vivo* and *in vitro*. We have engineered a *Salmonella typhimurium* vaccine strain that delivers the NY-ESO-1 tumor antigen through its type III protein secretion system. Sal-NY-ESO-1 efficiently elicited NY-ESO-1-specific CD8+ and CD4+ T cell responses *in vitro*. Oral administration of Sal-NY-ESO-1 to mice resulted in the regression of established NY-ESO-1-expressing tumors. Tumor regression was significantly accelerated in NY-ESO-1 DNA-primed animals. Epitope spreading to at least two tumor antigens not contained in the vaccine was observed in vaccinated animals. We propose that tumor-antigen delivery through the *Salmonella typhimurium* type III secretion system constitutes a promising novel strategy for cancer vaccine development.

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