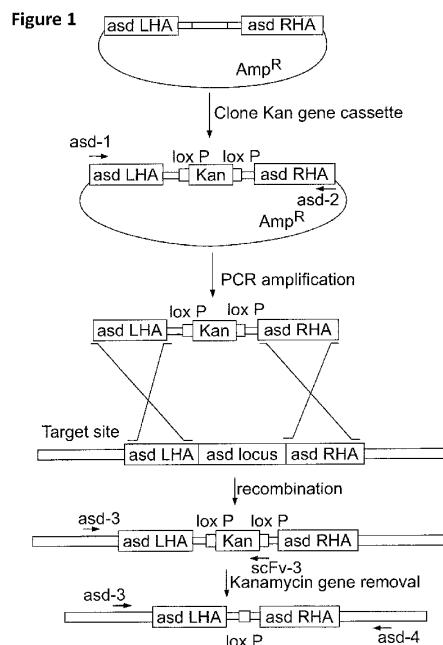




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(54) **Title:** ENGINEERED IMMUNOSTIMULATORY BACTERIAL STRAINS AND USES THEREOF

(57) **Abstract:** Provided are delivery immunostimulatory bacteria that have enhanced colonization of tumors, the tumor microenvironment and/or tumor-resident immune cells, and enhanced anti-tumor activity. The immunostimulatory bacteria are modified by deletion of genes encoding the flagella or modification of the genes so that functional flagella are not produced, and/or are modified by deletion of *pagP* or modification of *pagP* to produce inactive PagP product. As a result, the immunostimulatory bacteria are flagellin⁻ and/or *pagP*⁻. The immunostimulatory bacteria optionally have additional genomic modifications so that the bacteria are adenosine or purine auxotrophs. The bacteria optionally are one or more of *asd*⁻, *purT*⁻ and *msbB*⁻. The immunostimulatory bacteria, such as *Salmonella* species, are modified to encode immunostimulatory proteins that confer anti-tumor activity in the tumor

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microenvironment, and/or are modified so that the bacteria preferentially infect immune cells in the tumor microenvironment or tumor-resident immune cells and/or induce less cell death in immune cells than in other cells. Also provided are methods of inhibiting the growth or reducing the volume of a solid tumor by administering the immunostimulatory bacteria.