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# Flagellin mutant of *Salmonella typhimurium* VNP20009 producing recombinant mouse PD-1 preserves the growth kinetics and mobility of the parental strain

**Edyta Zyla, Mateusz Wawro** and **Joanna Bereta**
Jagiellonian University, Poland

The interaction of PD-L1 with T cell PD-1 receptor leads to the inactivation and death of T cells resulting in immunosuppression and undisturbed tumor development. We engineered *Salmonella* strain to deliver soluble PD-1 into tumor tissue. In principle, soluble PD-1 will compete with the PD-1 receptor on the T cell surface for binding to the PD-L1 ligand present on the surface of tumor cells and thus prevent T cell inactivation. The main goal of this work was to modify *Salmonella* therapeutic strain so it will be capable of efficiently secreting soluble PD-1 through the flagellar system. The flagellar system functions as a bacterial mobility motor but also serves as a secretory system for the extracellular elements of the flagellum. Special secretion signals direct certain proteins for flagellar channel-mediated secretion. To use the flagellar system for the secretion of recombinant proteins bacteria should be deprived of flagellin synthesis. To achieve this, we removed the fliC gene coding for flagellin monomer from the VNP20009 chromosome by homologous recombination and transformed the new strain with a plasmid coding for soluble PD-1 equipped with a suitable secretion signal. At present we are testing various secretion signals for optimal synthesis and secretion of PD-1 via the flagellar system. Interestingly, the characterization of the ΔfliC strain showed similarities characteristics to the parental one in terms of viability and growth kinetics. What is more, the mobility of the modified bacteria and the wild-type VNP20009 did not differ. However, the exposure of RAW264.7 cells to both *Salmonella* strains revealed that ΔfliC bacteria are less infective when compared to the parental strain. Nonetheless, in this case, the decreased cell infectivity might be beneficial as it will allow secreting PD-1 to the extracellular environment, where it may fulfill its anti-immunosuppressive task.

## Biography

Edyta Zyla has been started her PhD studies at Jagiellonian University in Kraków. From the very first beggining of Bachelor studies she was gripped by *Salmonella* using in anticancer immunotherapy. She was chairing student project and currently she is beneficiary of project financed by Biophysics, Biochemistry and Biotechnology Department UJ. To expand her horizons she has started working in Protein Crystallography Laboratory.

edyta.e.zyla@gmail.com

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