

**Filamentous bacteriophage: an old tool for a new nanovaccine.**

Filamentous phages are not lytic bacteria viruses that infect almost Gram-negative bacteria. They are widely distributed in many habitats of the world, having a constant relationship with human beings. Over the past three decades, phage research has had a renewed interest and bacteriophages have been employed in a large numbers of applications including therapy of bacterial infections, analysis of ligand-receptor interactions, and gene delivery.

We have exploiting the phage display technology to design a phage-based vaccine that express antigenic determinants at high density on the coat surface, together with a scFv directed against the dendritic cell surface receptor DEC-205, to target bacteriophages specifically to dendritic cells. The administration of targeted bacteriophages displaying antigenic epitope induces strong CD8 + T-cell responses in absence of adjuvant coadministration, and is able to protect mice from tumor growth in a model of tumor-engrafted mice. In addition, we observed induction of proinflammatory cytokines and type I interferon by fdsc-aDEC, in a mechanism dependent by TLR9 and MYD88 molecules.

RNA-Sequencing (RNA-Seq) analysis demonstrate a significant gene modulation in dendritic cells pulsed with targeted bacteriophages, indicating that filamentous bacteriophages activate many pathways linked to innate immunity. All these features make the phage a valuable tool to be used as a platform for antigen delivery in order to construct a vaccine that is able to activate and sustain a long-lasting adaptive immune response.

**Key publications:**

D'Apice L, Costa V, **Sartorius R**, Trovato M, Aprile M, De Berardinis P. Stimulation of Innate and Adaptive Immunity by Using Filamentous Bacteriophage fd Targeted to DEC-205. *J Immunol Res.* 2015; 2015:585078.

**Sartorius R**, D'Apice L, Trovato M, Cuccaro F, Costa V, De Leo MG, Marzullo VM, Biondo C, D'Auria S, De Matteis MA, Ciccodicola A, De Berardinis P. Antigen delivery by filamentous bacteriophage fd displaying an anti-DEC-205 single-chain variable fragment confers adjuvanticity by triggering a TLR9-mediated immune response. *EMBO Molecular Medicine.* EMBO Mol Med. 2015 Apr 17;7(7):973-88.

**Sartorius R**, Bettua C, D'Apice L, Caivano A, Trovato M, Russo D, Zanoni I, Granucci F, Mascolo D, Barba P, Del Pozzo G, De Berardinis P. Vaccination with filamentous bacteriophages targeting DEC-205 induces DC maturation and potent anti-tumor T cell response in absence of adjuvants. *European Journal of Immunology.* 2011, Jun 20.

**Sartorius R**, Pisu P, D'Apice L, Pizzella L, Romano C, Cortese G, Giorgini A, Santoni A, Velotti F, De Berardinis P. The use of filamentous bacteriophage fd to deliver MAGE-A10 or MAGE-A3 HLA-A2 restricted peptides and to induce strong anti-tumor CTL responses. *Journal of Immunology.* 2008; 180(6): 3719-28.

De Berardinis P, **Sartorius R**, Fanutti C, Perham RN, Del Pozzo G, Guardiola J. Phage display of peptide epitopes from HIV-1 elicits strong cytolytic responses. *Nature Biotechnology* 2000; 18(8): 873-876.