



**RESEARCH TOPIC-MEM16**  
**DISEASE SPECIFIC UNIVERSAL VACCINES AS NEW COMBINATORIAL IMMUNOTHERAPY FOR METASTATIC MELANOMA SARCOMA AND OSTEOSARCOMA**

**Curriculum MEM Standard**

**Laboratory name:** Mucosal immunology and microbiome unit, Humanitas University

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**Abstract**

Despite immune checkpoint blockade (ICB) has drastically changed the prognosis of previously untreatable tumors, a considerable fraction of patients is refractory to therapy. ICB reactivates T cells to recognize cancer presented antigens, and the general consensus is that resistant patients lack pre-existing immune responses or downregulate the antigen presenting machinery. We have demonstrated that infection of tumor cells with Salmonella releases peptides, including those preferentially presented in cells deficient in the antigen presenting machinery (i.e., TEIPP), that prime shared anti-tumor immune responses. These responses are effective in controlling metastatic tumor growth with objective clinical response.

We hypothesize that vaccination of melanoma and sarcoma patients with disease-specific shared immunogenic peptides is a universal means to elicit anti-tumor immune responses capable of overcoming immune evasion strategies and anti-PD-1 resistance. In this project we will study the effect of vaccination in a clinical trial with a thorough immunomonitoring

**Main technical approaches**

Immunology techniques: ELISA, flow cytometry, cell proliferation, tumor specific T response; molecular biology techniques

**Scientific references**

1. Wolchok JD, et al. Nivolumab plus ipilimumab in advanced melanoma. The New England journal of medicine 2013;369:122-33
2. Gros A, et al. PD-1 identifies the patient-specific CD8(+) tumor-reactive repertoire infiltrating human tumors. J Clin Invest 2014;124:2246-59



3. Gao J, et al. Loss of IFN-g Pathway Genes in Tumor Cells as a Mechanism of Resistance to Anti-CTLA-4 Therapy. Cell 2016;167:397-404

4. Zaretsky JM, et al. Mutations Associated with Acquired Resistance to PD-1 Blockade in Melanoma. N EJ Med 2016;375:819-29

5. Ott PA, et al. An immunogenic personal neoantigen vaccine for patients with melanoma. Nature 2017;547:217-21

### **Type of contract**

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