

## **Title: Vaccines to overcome Therapeutic Resistance in Lung Cancer**

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**Research theme / topic:** Tumor immunology and cancer vaccines

### **Main Abstract:**

Non-small cell lung cancer (NSCLC), 80-85% of all lung cancers, is associated with a poor prognosis and late diagnosis. The introduction of targeted therapies and immunotherapy in clinical practice has redefined treatment options for this disease. Nevertheless, the onset of drug resistance is still the major obstacle to treatment success. Cancer vaccines represent a promising alternative therapeutic route for patients experiencing relapse or with no other treatment options.

The goal of this project is the definition of a panel of antigens exploitable for the development of vaccines against lung cancer and will be reached through the study of distinct clinical conditions:

- i. Translocations of ROS1 gene, prevalence of about 1-2%, are neoantigens with a driver role and exposed in the extracellular compartment. ROS1 fusions will be studied for their immunogenic properties. In silico design of vaccines based on immune-reactive epitopes and in silico trials will be performed. Furthermore, custom recombinant monoclonal antibodies against specific epitopes will be in vitro tested on ROS1-fusion positive patient-derived NSCLC cell lines.
- ii. Activating EGFR mutations were found in 10-15% of NSCLC patients. Over time, however, patients develop mechanisms of resistance due to the onset of new EGFR mutations. Autoantibody and circulating T cell reactivity against EGFR wild-type and mutated epitopes will be evaluated. Plasma and PBMCs will be collected from patients with EGFR-mutated NSCLCs at different time points during the treatment schedule. Epitopes inducing high B and T reactivity will be considered for in silico vaccine testing.
- iii. NSCLC cells from immunotherapy-resistant patients present a high stemness. Databases will be queried to find candidate antigens associated with alterations of stemness and EMT markers. Then, the driver role of candidate genes, an essential requirement for cancer vaccine development, will be investigated by modulating antigen expression (silencing or overexpression) in NSCLC primary cell cultures.



By Dr. MS. Semprini and C. Falchieri

**Techniques.** Cell cultures: achievement of primary cultures from tumor biopsies, 2D and 3D growth tests, transfection, silencing, cloning. Molecular analysis: immunofluorescence, flow cytometry, Real-Time PCR, Western Blot, ELISA test, ELISPOT. In silico analysis will be performed in collaboration with Prof. Francesco Pappalardo (Combine group, University of Catania) and the PI will support the participation of the PhD student to a course to encourage him/her to improve his/her abilities in the analysis of public databases (e.g. C-Bioportal).

Palladini et al. Oncoimmunology 2018, Angelicola et al., Cancers 2021