

Short Descriptions of Research Projects

Prof. Laurence Zitvogel, MD PhD, Gustave Roussy Comprehensive Cancer Centre, Villejuif, France

How the gut microflora influences the efficacy of new anti-cancer treatments

(Original title: Impact of gut microbiota in the efficacy and toxicity of immune checkpoint blockers in oncology)

Last year, progress in immunotherapy changed the landscape in oncology. New antibodies that help redirect the immune system to attack the tumour are now available: They are called immune checkpoint blockers, the first available being ipilimumab. They showed a broad potential and trials in many tumour types have been initiated. These drugs can achieve durable disease control, even in advanced cancers. Unfortunately, they do not work in all patients and some patients show severe adverse effects limiting their broad use.

Prof. Zitvogel recently showed that the gut microbiome composition, meaning the composition of the bacteria in our guts, has a profound influence on the efficacy and toxicity of those antibodies. She plans to explore the reasons for this and in a second step to validate the relevance of the findings in patients. Uncoupling efficacy from toxicity represents a challenge and an unmet medical need and is highly relevant for cancer control as checkpoint blocking is one of the most promising new treatments for cancer.

Prof. Adrian Ochsenbein, MD, Department of Medical Oncology, Inselspital, Bern University Hospital

Targeting the cancer-initiating cells

(Original title: Targeting TNF receptor TNIK signalling to eliminate cancer stem cells)

In recent years, the understanding of cancer biology has fundamentally changed. While it was previously assumed that tumours represent a group of similar ever-proliferating cells, it has been recognized in the last 10 years that the tumours are formed from various cell types having different functions and potentials, and that the cells are organized hierarchically. In various tumour types, it was shown that only a small number of the cancer cells have the ability to maintain tumour growth over a long period of time, while most of the cancer cells only have a limited life span. These disease-initiating cells are called cancer stem cells, abbreviated CSCs. They self-renew and give rise to the other cells in the tumour. From a clinical point of view, CSCs are of fundamental interest since these cells are resistant to most of the current cancer treatments and might be responsible for disease relapses.

Resistance of CSCs to treatment is mediated by cell intrinsic characteristics but also by the interactions of the cells with their microenvironment. This is best documented for leukaemia stem cells that depend on signals from their surrounding environment to maintain stem cell characteristics. The immune system is an important part of the tumour microenvironment and may contribute to tumour control.

Over the last years, the laboratory of Prof. Ochsenbein has been investigating the mechanisms by which the immune system contributes to the progression of solid tumours and leukaemia. They recently documented that a signalling pathway is crucially involved in the formation of leukaemia as well as other solid tumours including colon cancer. This signalling pathway is called the TNFR/Wnt signalling pathway; it is a hallmark of CSCs and is necessary to maintain several important stem cell characteristics. Built on their previous work and new technical developments they will analyse the role of this signalling pathway in leukaemia stem cells and in colorectal CSCs. These experiments will investigate the possibility of manipulating this signalling pathway in order to target CSCs. This is of prime importance as it is becoming clear that the cure of cancer implies the elimination of cancer stem cells.