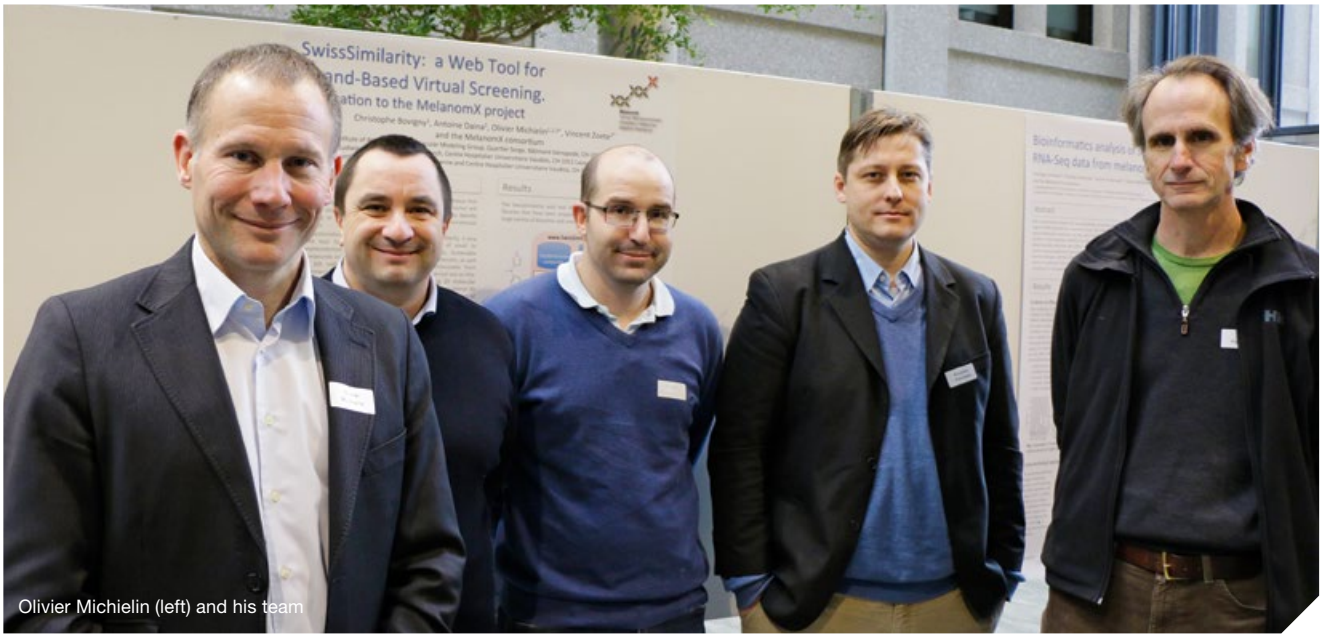

Olivier Michielin (left) and his team

3. MelanomX – Deciphering the mechanisms of resistance

As with other types of cancer, significant progress has been made in the treatment of melanoma over the past few years. Unfortunately, all affected patients experience resistance to the drugs after some time. The MelanomX project is searching for the cause of this resistance.

The successful use of drugs to inhibit the BRAF-oncogene was one of the most significant victories in the treatment of advanced melanoma. In spite of this, patients are still experiencing the development of resistance after about six months. Olivier Michielin, professor at University of Lausanne, and his team working on the MelanomX project are examining the mechanisms employed by cancer cells in order to develop better therapies.

Using a systems biology approach, the researchers want to decipher the resistance to BRAF inhibition (BRAF is a protein that promotes tumor growth) on the single-cell level. The researchers have developed a way of determining the complete mutational landscape of thousands of single cells from metastatic melanomas. They are studying samples taken from patients before and during BRAF inhibition, as well as patients whose therapy failed or led to disease progression. In this way, the scientists want to interpret the dynamics of resistance.

"In order to carry out this study, we first had to improve our technical equipment so that only single cells were examined, as opposed to several cells at once, which would cloud the results," says Michielin. The researchers also noticed that the frozen cancer cells they studied yielded far inferior results than the fresh samples. "We have discovered that these cancer cells are very temperature sensitive. Fresh samples are of much better quality, meaning that we have had to adjust our whole workflow. The process has become more complicated, as everything has to be done much faster," reports Michielin. After analyzing thousands of single cells, the team has managed to describe the cellular composition of melanoma in great detail and has already identified a number of potential targets for therapy.

"In the next step, we will test a number of different molecules that work to block various mechanisms within the cancer cells," explains Michielin. This could be the first step towards the development of new medication, and therefore to a sustainable treatment for melanoma.

MelanomX at a glance

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MelanomX
Tumour Microenvironment Crosstalk in Melanoma Adaptive Resistance