Project title: Multi-onco-map: a multi-omic map of major oncogene function in cancer.

Cancer is one of the main reasons of deaths in western countries. In recent years improvement in diagnostics and therapeutic protocols caused increased patient survival in many types of cancer, while others still remain resistant to modern therapies. Cancers of lung, large intestine and pancreas will contribute to most deaths in the EU countries in the upcoming years. Novel therapies that target major oncoprotein "drivers" of these cancer types are either inefficient or prone to resistance mechanisms and allow cancer to progress and metastasize. It is a paradoxical situation that the scientists know for decades the main molecules responsible for driving the cancer progression – such as mutant p53, Ras or Myc oncoproteins – and are still unable inhibit them using efficient drugs.

The following project attempts to solve this problem by learning the details of the molecular programs of those major oncoproteins which drive cancer cell transformation and aggressiveness. Three different oncogenes will be removed by genetic engineering using CRISPR-Cas9 method from cancer cells grown *in vitro* of the three most deadly cancer types. Then, the RNA and protein content of these cells will be measured by the most sophisticated of the available large-scale methods in modern biology – new generation sequencing of RNA and whole cell proteomic analysis. The collected data, after bioinformatics analysis, will first allow to understand which genes and proteins are controlled in the cells by the studied oncogenes. The inclusion of three cancer types and three oncogene types will next allow to map where the molecular programs of the oncogenes intersect in multiple cancer types and where they possess specific features (hence the project name: Multi-onco-map). Both universal and specific oncogenic programs will be further used to select potential molecular nodes of oncogenic signaling which can be targeted by new drugs or already known ones in new contexts. A few of the most promising treatment protocols arising form the multi-onco-map will be tested already in this project, including drug tests in organ-like structures (organoids) derived from Polish cancer patients.

Thus the multi-onco-map will become a valuable source of information about molecular hubs and spokes of oncogenic signaling across several cancer types and will potentially be a source of several new therapeutic protocols to help save lives of cancer patients.