# A tissue-engineering platform for precision cancer medicine and in vitro chemosensitivity testing for head & neck squamous cell carcinoma (HNSCC)

In Poland, head & neck cancer cases have been increasing in the 15 years between 1999 and 2014 by over 20%, from approx. 8,700 to 11,600 cases per year. To make things worse, head & neck cancers are also often detected at a late stage, which makes it much more difficult to treat these patients. This happens in over 60% of the cases and reduces the chance of the patients to be cured by operation, radiation therapy, or chemotherapy. Many of them die within just 1 year after therapy. In average, between 40 and 60% of the patients survive for more than 5 years. Their survival also depends strongly on where they are treated – in cancer centres, located in the large cities, survival is much better (60%) than in smaller medical facilities (survival around 40%). Head & neck cancers belong to the tumours for which both diagnosis and therapy would need to be improved, and most likely can be improved – by different strategies. The best strategy would be earlier detection of these tumours. But for the many patients who are still showing up with advanced cancers, any strategies for improving different forms of therapy would be extremely beneficial. Unfortunately, there are not that many different forms of treatments and drugs available. Therefore, it would also be very interesting to test new forms of therapy, or combinations of standard anti-cancer medicines with new drugs, hoping that this may result to more successful treatment.

The numbers indicate that there is much room for improvement of therapy for patients with head & neck cancers. For this, it is typically important to classify the patients into different classes or categories according to their drug response – which is called "stratification" in clinical practice. Stratification is one important aspect of "precision medicine", in which clinicians try to get the optimal form of therapy to patients that are most likely to benefit from it. It also means that it may be better to spare patients from aggressive forms of therapy, if they are not likely to respond to it. Much unnecessary suffering and poor quality of live could be avoided. The most common strategies for stratification, or selecting patients for certain forms of therapy, includes the genetic analysis of the patients' tumours. Certain genetic mutations can be associated with better or worse survival. In many cases, however, it is not well understood, how the presence or absence of mutations, often many of them at the same time, influences how a patient responds to therapies. Genetic analyses are not only costly for the public healthcare system, they are most likely also not sufficient to predict if a patient responds to a certain therapy, or not. It would be very beneficial if different therapies, in particular the anti-cancer drugs used in chemotherapy, could be tested before they are given to patients. This currently represents a technical problem and is not widely used (or not at all) in clinics. There are many reasons for this: it is simply difficult to grow the patients' tumour cells outside the tumour – the standard conditions in culture are very different to the real tumours, and tumour cells do not tolerate these changes very well. It is also not known if the cells that would grow in such cultures are really the same that are seen in the original tumour – and are responsible for the drug response. The cell culture conditions may lead to the selection of different populations of tumour cells, that may respond very different to drugs, than the original cancer tissues.

The project has the goal to improve this situation. We will define the best cell culture conditions for primary tumour cells in such a way, that we can guarantee that the right cells are present, and that these cells respond to the therapy in much the same way as those in the patients' original tumour. This will require a large amount of optimization of cell culture conditions, but hopefully will be worth it. We will explore many different ways how to grow these tumour cells, in a different "environment". For this, we will use technologies from "tissue engineering" to optimize how tumour cells can be cultured outside the body – and used for these tests. The idea is to expose the tumour cells to conditions that are very similar to those inside the original tumours. Under these conditions, tumour cells would be expected to also react in a similar way to drugs as the original cancers. If these tests are really predictive for the patients' response, they could be used as a valuable method to select useful therapies before patients are exposed to them. This will be a way to a) identify drugs that are likely beneficial for the patients, and b) to prevent that patients are exposed to chemotherapies that are not effective, but only cause suffering and serious side effects. The same tests can also be expanded, and a larger number of anti-cancer drugs can be tested, including new ones that are not yet used in the clinics. Such drugs could also be combined with each other, and combinations be identified that are more beneficial for patients than each of the single drugs on their own. This project has a strong potential to improve therapy for head and neck cancer patients, and also to discover new drugs or therapies.