WHEN THE TREATMENT DEPENDS ON THE PATIENT'S GENES

Our risk of suffering from various illnesses is encoded in our genes, and so is how our organism will respond to certain treatment. This is why, in oncology, certain modern drugs are administered only to carefully selected patients who carry certain mutations which are targeted by the medicine. But this principle does not apply only to treatment of cancer. Personalized medicine, in which the course of therapy depends on the results of genetic diagnostics, is increasingly used also in other illnesses, e.g. cardiovascular.

Dr Anna Wójcicka, CEO of Warsaw Genomics, a company operating at the University of Warsaw, laureate of the TEAM TECH programme (4/2017) of the Foundation for Polish Science, is working on a genetic test for use on patients with thrombotic microangiopathies (TMA).

TMAs are a group of illnesses which lead to the development of thrombosis in capillaries and arterioles. The process of thrombosis in small blood vessels results from injury to the lining of the blood vessels, which in turn may result for example from infection or auto-aggression. The thrombosis developing in the capillaries blocks micro-circulation, and the hindered flow of blood and other structural changes lead to damage to internal organs, particularly the kidneys.

According to Dr Wójcicka, "The kidneys perform several key functions in the organism, first and foremost cleansing the organism of toxins. So they are essential for life. Extreme deficiency in kidney function is life-threatening, and if we do not implement kidney replacement therapy (dialysis or transplant), it will soon lead to death. This also applies to patients with TMA."

As Dr Wójcicka explained, "What is particularly important is that the clinical course of TMA, including the success of a kidney transplant, depends on the patient's genetic profile. In the presence of

certain genetic mutations, the risk of recurrence of the disease in the transplanted kidney is over 80%, and thus the operation should not be conducted. Identifying patients for whom transplantation of an organ will not achieve the hoped-for results is vital from the perspective of all patients waiting for that organ. In Poland the waiting time for a kidney transplant is about two years. Every year about 2,500 people are added to the waiting list and about 1,000 patients receive a transplant. This makes it crucial that transplants are received by patients for whom the treatment can be expected to succeed. Genetic diagnostics of patients with TMA can help achieve this. This diagnostic is currently recommended but unfortunately is not widely available."

The company headed by Dr Wójcicka, Warsaw Genomics, is involved in creating and providing to doctors and patients the most sensitive and precise genetic tests possible, based on the latest achievements of world science. It is currently the only unit in Poland conducting genetic diagnostics of patients with TMA, but the process is time-consuming, arduous and costly. Moreover, research has shown that the course of TMA in the Polish population may be conditioned by the presence of somewhat different genetic mutations than in other populations.

"That is why our intention is to develop a comprehensive diagnostic test especially for Polish patients, enabling a determination of the risk of loss of a transplanted kidney among patients with thrombotic microangiopathies," said Dr Wójcicka. "During the course of the project we will identify genetic mutations not previously described whose presence increases the risk of development of TMA. This will be made possible through cooperation between Warsaw Genomics and the Clinic of Transplantation Medicine, Nephrology and Internal Medicine at the Medical University of Warsaw, headed by Prof. Magdalena Durlik. We also hope for wider cooperation with other units. Based on the results we generate, a genetic test will be developed enabling a quick and complete diagnosis of patients with TMA, and an algorithm will also be created for forecasting the clinical course of the illness."

Dr Wójcicka, a winner of the TEAM TECH programme (4/2017) (conducted by the Foundation for Polish Science under the Smart Growth Operational Programme), previously implemented another grant from the foundation under the IMPULS programme (3/2014) (part of the FNP SKILLS project). That project involved the launch of a complex molecular test to predict the risk of death from thyroid cancer. The test made it possible to more effectively identify patients with thyroid cancer who were most at risk of an aggressive form of the disease.

"In about 90% of cases of thyroid cancer the course of the illness is mild and patients can live for decades without recurrence of cancer," Dr Wójcicka explained. "But in about 10% of patients, the illness proceeds very aggressively, quickly leading to metastasis and death. These people should be treated very intensively from the very onset, among other things by removing their entire thyroid. Our aim was to develop a method for stratifying patients into different risk groups and adjusting the scope of treatment accordingly."

Initially the researchers identified five molecular markers significantly contributing to the risk of death in the patient, and during further research they found one gene where a mutation translates into an exceptionally aggressive spread of the cancer. "On that basis we created a molecular test for forecasting the clinical course and thus developing a personalized approach to the thyroid cancer patient," Dr Wójcicka said. "We perform the test based on an analysis of the genes in a blood sample,

before the operation. Based on the test results, the surgeon knows whether to operate on the patient radically, by removing the entire thyroid, or it will suffice to remove the one lobe of the thyroid gland where the cancer appeared. Removing only one lobe is highly advantageous because the patient does not have to take hormones for the rest of their life and is also much less at risk of complications during the operation."

Dr Anna Wójcicka is the CEO of Warsaw Genomics. She also works at the Laboratory of Human Cancer Genetics at the Centre of New Technologies at the University of Warsaw and the Laboratory of Genomic Medicine at the Medical University of Warsaw. She earned her doctorate in medicine at the Centre of Postgraduate Medical Education in Warsaw and her postdoctoral degree at the Medical University of Warsaw. She also completed postgraduate studies in innovation management at the Warsaw School of Economics. She has held research fellowships at the Department of Medical Genomics at Vrije Universiteit Amsterdam, the Molecular Endocrinology Laboratory at Imperial College London, and the Ohio State University Comprehensive Cancer Center in the US. She is the winner of awards and fellowships from the Minister of Science and Higher Education, the Federation of European Biochemical Societies, the British Society for Endocrinology, the European Thyroid Association, the Minister of Health, and the Foundation for Polish Science. She was named a Very Important Polish Innovator by the Teraz Polska Foundation. She has co-authored numerous scientific publications on the genetics of human illnesses and directed numerous research projects in this area. Her mission is to popularize genetic testing among Poles as an element of preventive healthcare, diagnostics, and targeted therapies.

Pictured: Dr Anna Wójcicka and her team (source: www.badamygeny.pl)