NEW THERAPEUTIC APPROACHES FOR HEMOGLOBIN DISORDERS

Treatments for sick blood cells

If our red blood cells cannot transport enough oxygen, the whole body suffers as a result. Organs become undersupplied or may even fail. A genetic mutation in the oxygen transporter hemoglobin is often the root cause of diseases which are categorized under the medical term hemoglobinopathies. Current treatment options are limited, however, and often associated with side effects. Scientists at Bayer HealthCare are therefore working on new therapies to help patients with hemoglobinopathies.

Our blood transports oxygen and nutrients to each individual cell. Roughly half of the blood volume is made up of cells, primarily red blood cells (erythrocytes). These cells use the red blood pigment hemoglobin, an iron-containing protein, to transport oxygen: like a molecular vessel, it collects this essential gas in the lungs and delivers it to the cells and organs throughout the body. Some people have an inherited mutation in their hemoglobin gene that may prevent the efficient transport of oxygen. “These individuals produce a ‘faulty’ version of the blood pigment called sickle hemoglobin or hemoglobin S, which is not able to transport the same amount of oxygen as the normal form. This condition is called sickle-cell anemia, because the red cells are shaped like a sickle,” says Dr. Katalin Kauser, Head of Hematology Research at Bayer HealthCare in San Francisco’s U.S. Innovation Center. Sickle cells are stiff and sticky and tend to block the blood flow in the blood vessels of organs, which then receive an insufficient supply of oxygen, causing patients to become more quickly fatigued. In more severe cases, however, the small blood vessels can occlude, causing pain and organ damage. “This can lead to organ failure. The life expectancy of patients with sickle cell disease is only 40 to 50 years. Devastating pain crises are part of their lives,” explains Kauser.

Sickle-cell anemia is the most common and severe hemoglobinopathy. Seven percent of the world’s population carries the gene mutation responsible for this condition. It is particularly common in the regions at the equator – in some areas, more
than 19 in every 1,000 newborn children are affected. At present there is only one drug therapy approved for the condition. It was originally developed to treat cancer and is able to reduce the number and severity of the pain crises. “And there is also a cure for this disease: a bone marrow transplant,” explains Kauser. “However, it is difficult to find a matching donor and there are risks associated with it.” Since 2012, Bayer scientists have been working closely with the UCSF Benioff Children’s Hospital Oakland, California. This hospital is one of the leading centers of academic research on hemoglobinopathies in the United States and the largest clinical center for sickle-cell disease on the West Coast.

The scientists and physicians at UCSF Benioff Oakland are working together with the Bayer teams to develop a therapy for sickle-cell anemia. “Due to their sickle shape, red blood cells of affected individuals are fragile and shorter-lived,” says Kauser. In contrast to healthy, disk-shaped blood cells, they easily perish in circulation and release their hemoglobin. The broken cells and the excess amounts of the iron-containing red pigment have to be removed from the blood as they would otherwise damage organs such as the heart. “We want to help the body to carry out this ‘detoxifying’ process. Our team is working on novel ideas to decrease the concentration of hemoglobin degradation products in the blood,” explains the Bayer scientist. This should help the liver and spleen to manage the overload and protect the different organs against damage. “At present we are comparing the measurements from tests with cell cultures and animal models with the values from real-life patient samples from UCSF Benioff Oakland,” says Kauser, summarizing the current status. “If it all goes according to plan, we might soon be able to take a first active substance into early-stage clinical testing.” This treatment could relieve the symptoms of sickle-cell anemia, which for sufferers would already be a huge relief. “But our long-term objective for drug development is in fact to cure this disease,” says Kauser. She and her team are therefore also exploring novel forms of therapy that work directly at the gene level.

The scientists at Bayer are also investigating another type of hemoglobinopathy, a disease called thalassemia. In this condition, the erythrocytes look normal from the outside but in fact they carry a mutated blood pigment. Patients suffering from thalassemia also produce abnormal hemoglobin, causing rapid breakdown of blood cells. The current therapy for these patients consists of repeated blood transfusions to manage the resulting anemia. However, with every transfusion, the iron bound in the red blood cells is also transferred, which the body of thalassemia patients cannot actively eliminate. “This leads to an excess of iron, which is taken up by different organs including the liver, heart or kidneys. Excess iron in the organs can lead to damage and ultimately organ failure,” explains Kauser. Her group, together with the experts from the UCSF Benioff Oakland, is therefore also focusing its work on regulating the uptake of iron into the blood.

The Bayer scientists are contributing their experience in development of active substances to the collaboration, while UCSF Benioff Oakland is sharing its comprehensive research knowledge and clinical experience with patients. “We recently extended the agreement with UCSF Benioff Oakland by two more years,” says Dr. Lisa Mendoza, Associate Director of the U.S. Science Hub of Bayer HealthCare and Alliance Manager of the collaboration. If the research path that the experts of Bayer and UCSF Benioff Oakland have taken is successful, hemoglobinopathy sufferers could soon be able to get back some quality of life. After all, being able to relieve the symptoms of these diseases and in the future possibly even cure them is a promising prospect.

www.research.bayer.com/hemoglobinopathies

More information on this topic

Distribution of sickle-cell anemia

Many people living near the equator suffer from sickle cell anemia. Africa is particularly heavily affected.

Fighting pain together: Dr. Katalin Kauser and her team are working to alleviate the pain suffered by hemoglobinopathy patients.