New drugs to combat asthma and the like

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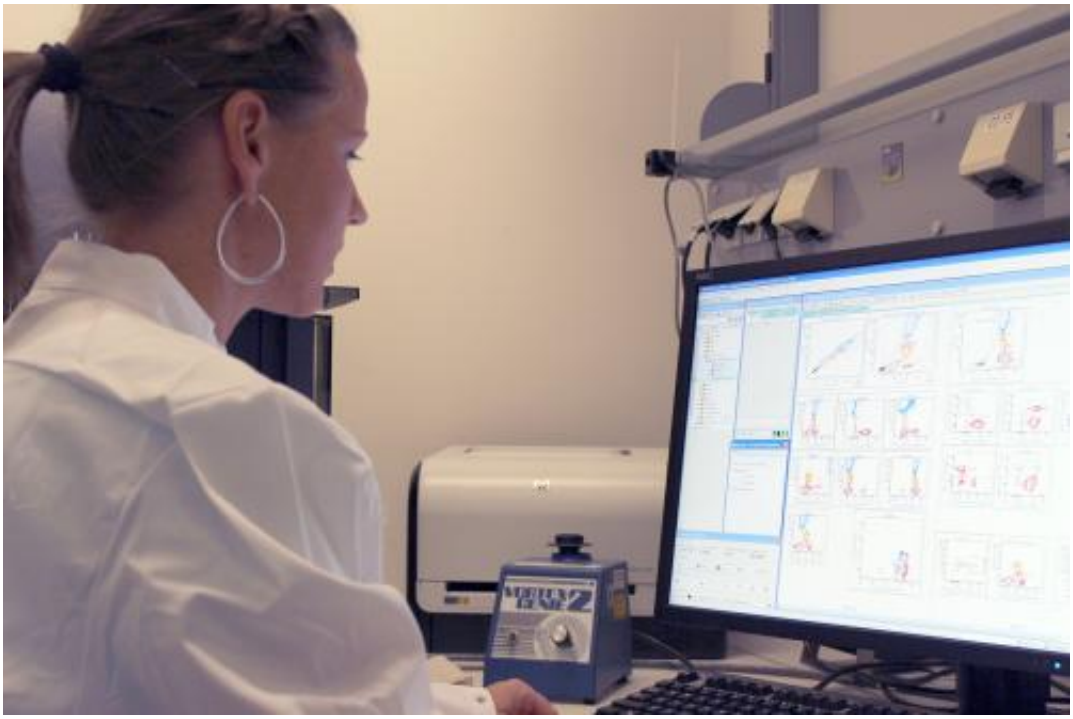

Science and industry are collaborating to develop future pharmaceuticals for treating chronic inflammatory diseases. The medicines will combat immunological processes that have gone wrong. The researcher analyses immune cells in order to ascertain the effects and side-effects of the new drugs. Credit: Fraunhofer IZI

Science and industry are collaborating to develop future pharmaceuticals for treating chronic inflammatory diseases. The medicines will combat immunological processes that have gone wrong.

Statistics indicate that there are 300 million asthma sufferers worldwide, a further 600 million people living with chronic pneumonia and up to 30% of the global population contending with allergic rhinitis (allergic inflammation of the nasal airways). Chronic inflammatory diseases can also affect other organs and parts of the body beyond the respiratory system; they can occur in the intestine (in the form of inflammatory bowel diseases such as colitis ulcerosa), the joints (rheumatoid arthritis), the skin (scleroderma), or the heart and blood vessels (arteriosclerosis). What each form of inflammatory disease has in common is that it stems from centers of inflammation in the body that are prevented from healing by immunological processes that have gone wrong.

This is where a new product made by the Canadian company Nuvo Research Inc. comes in. It is already approved for use in many countries around the world as a drug to assist local wound healing, and in Thailand is already sanctioned as a means to treat a variety of chronic diseases. Scientists at the Fraunhofer Institute for Cell Therapy and Immunology IZI in Leipzig are now working with a German subsidiary of the company, Nuvo Research GmbH, and the Translational Centre for Regenerative Medicine TRM at Leipzig University to develop a platform that will enable them to better understand the way the substance works. Their objective is to optimize the drug to make it more convenient to administer and better tolerated. Above all, the scientists are keen to develop derivatives of the drug with which it might be possible to alleviate an even broader range of chronic illnesses, and to prepare these drugs for approval on the European and Canadian markets. The cooperation project, sponsored to the tune of 4.4 million euros, is due to be completed in June 2014.

Regenerative process disrupted in the case of chronic inflammation

"Inflammation is the body's emergency response, but inflammation normally begins to abate the moment it starts. In order for the organism to calm back down and stabilize, the immune system is temporarily suppressed. The body suppresses its defense mechanisms until the inflamed tissue has managed to regain its normal functions. This regenerative process is disrupted in the case of chronic inflammation," explains Professor Jürgen Arnhold, who is based at Leipzig University's Faculty of Medicine and also conducts research at the TRM. Various complications can occur, such as bacterial or fungal infections and disruptions to the wound healing process. If such complications develop beyond a certain threshold, the immune system will suddenly leap back into action very violently. It is this interplay between immunosuppression and immunological overreaction that the scientists are looking into as part of the project. There is clearly a class of enzymes at work that would normally be activated by immune cells within a very specific time window. If this activation occurs in an uncontrolled manner, the last phase of the inflammatory process is disrupted and becomes chronic. This is where the particularly small, low-molecular substance developed by Nuvo comes in: "Studies we conducted on isolated immune cells indicate that it should be possible to change the function of some of the enzymes involved," says Professor Arnhold.

Where scientists at the TRM are investigating the way selected immune cells react to the Canadian drug, researchers at the IZI are interested in looking at its effect on the organism as a whole. The reason for these investigations is that in order for the drug to be approved in Europe and North America, authorities demand that complex and time-consuming studies be conducted into its safety, tolerability and effectiveness. "We test the medication on mice that display the same sorts of symptoms of illness as patients with chronic inflammatory diseases," explains Dr. Franziska Lange, head of the Inflammation Models and Immunodiagnostics Unit at the IZI. "My working group focuses on three conditions: asthma, smoker's lung and scleroderma, an autoimmune

connective tissue disease. We established 20 different model systems with which we are able to simulate different aspects of inflammatory diseases. This enables us to record the effects and side-effects of different doses of the drug on mice. We see ourselves as a service unit and offer many different ways to carry out preclinical tests on potential pharmaceuticals," she goes on to explain. A further three IZI working groups are testing the drug on mice who have suffered a stroke or who have colitis to see whether the animals' symptoms improve. They are also investigating whether the drug might be useful in treating breast cancer.

The three cooperation partners have already conducted two studies and both proved the effectiveness and safety of the basic active ingredient. Currently they are hoping to set up another project that aims to improve the method of application of the drug. In Thailand it is currently administered as an infusion, which means patients have to visit the clinic five days in a row for several hours at a time. The trio is working on preparing the drug in such a way that it can also be injected by family doctors.

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