Max Planck Institute of Biochemistry
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Anticancer Substances Clear Next Hurdle

Licensing Agreement Signed by the Max Planck Institute of Biochemistry, Lead Discovery Center GmbH and the Qurient Company

Most cancer patients die of the disease because tumor cells spread to other sites in the body and form new tumors, so-called metastases. Scientists of the Max Planck Institute (MPI) of Biochemistry in Martinsried and their cooperation partners of the Lead Discovery Center GmbH (LDC) have now signed a licensing agreement with the Korean company Qurient for a group of active substances that have been a focus of their research for a long time. These substances shall target metastasizing and drug-resistant tumors more specifically and selectively. Qurient will successively enter the tested substances into preclinical and clinical trials in order to use them in the future for drugs in patients. The Max Planck researchers hope that if the experiments and clinical trials are successful, a drug based on the new active substances could be on the market by the end of the decade.

According to the World Health Organization (WHO), cancer causes about 7.6 million deaths per year, making it the second leading cause of death in the world after cardiovascular disease. Therefore, there is a growing need for effective drugs. The new substances, which are the research focus of the three cooperation partners, belong to the family of highly specific Axl kinase inhibitors. In the research department headed by Axel Ullrich at the MPI of Biochemistry, the scientists Pjotr Knyazev and Robert Torka have been conducting research on the protein Axl kinase and its inhibitors for more than ten years.

The Axl kinase is a receptor protein that is found on the surface of many cell types. It recognizes specific signal substances that play a critical role in the survival and migration of cells. The researchers showed that fewer metastases develop when the Axl kinase is inactivated. In many aggressive types of cancer the Axl kinase is present at too high levels and is thus hyperactive. For this reason, the cells are constantly stimulated to grow or migrate.

“If we block the Axl kinase, we can prevent the cancer cells from migrating and forming new metastases,” said Robert Torka, explaining the effect of the new substances. The target that the inhibitors attack is located in the interior of the cell, at the Axl kinase domain. After the appropriate signaling substance is bound externally, an energy carrier (ATP) must additionally dock to the receptor internally before the signal can be transmitted to the cell nucleus. The new substances prevent the ATP from binding and the receptor from becoming activated and thus prevent the signal from reaching the cell nucleus. All Axl kinase-dependent processes are therefore blocked in the cancer cell.

Various groups of such inhibitors have already been patented at the MPI of Biochemistry. To make the individual substances even more effective against particularly aggressive,

metastasizing tumors, it was necessary to generate chemical variants. The Lead Discovery Center GmbH (LDC) assumed this part of the cooperation. For example, the LCD scientists altered the substances so that they were more soluble. The researchers at the MPI of Biochemistry then tested the variants on different cancer cell lines derived from the lung, breast or pancreas e.g. for tolerance, dosage or efficacy in combination with other active substances.

The Qurient Company will successively bring the substances to preclinical and clinical trials, in order to use them later as drugs. To continue to optimize the agents further, the scientists of the MPI of Biochemistry and the LDC are participating with tests and experiments for an additional year of collaboration. Afterwards both partners take over a consulting function during the whole development process. “Our common goal is to make tumor treatments more selective and targeted to the tumor cells. The new substances are a step in the right direction,” said Pjotr Knyazev, scientist in the Department of Molecular Biology at the MPI of Biochemistry. [VS]

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