No. 25c3 July 13, 2016 (Koh)

2016 Windaus Award for Dietrich Keppler

Dietrich Keppler, who was head of a research division at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) until 2007, has been awarded the 2016 international Adolf Windaus Award for his research achievements. Keppler, a biochemist, has made seminal contributions towards unraveling the molecular mechanisms of how substances are transported into the liver and from the liver into the bile. The Windaus Award has been given by the Falk Foundation since 1980 for outstanding achievements in the field of bile acid research. The award comprises €15,000.

The liver excretes many substances that are useless or toxic for the body into the bile. One of these substances, for example, is bilirubin, which is the metabolite of hemoglobin, the pigment in the red blood cells. If this excretion process is disrupted, blood levels of the yellow bile pigment bilirubin rise, resulting in jaundice. Keppler and his department elucidated the details of this substance transport.

Liver cells (hepatocytes) are equipped with various transporter proteins that mediate and regulate the import and export of substances. Keppler and the researchers working with him discovered that various members of the organic anion-transporting polypeptide (OATP) family are responsible for the absorption of bilirubin into the hepatocyte at the surface facing outwards towards the bloodstream. In contrast, various transporters of the multidrug resistance-associated protein (MRP) family facilitate the export into the bile canaliculi. Cancer researchers know these MRP transporters for their capability of pumping anticancer drugs out of tumor cells such that their levels in the tumor cell are often not high enough to be effective.

In addition to their function of facilitating substance transport from the liver into the bile canaliculi, transporter proteins play an essential role in the body. They are involved wherever substances and secretions are passed outwards via small channels or ducts, such as in the intestine or the mammary ducts. To enter these channels, all substances in the bloodstream intended for excretion must pass a layer of specialized epithelial cells that are equipped with transporter proteins.

Therefore, the results of Keppler's comprehensive molecular analyses are of substantial importance and have been used across the globe in the development of new drugs for many years. Whenever agents are directed at targets in the cell interior, pharmacologists initially make sure that the appropriate import proteins are present. To this end, it is crucial to know which transporter is responsible for which substance in the specific tissue. In addition, it is possible to use highly-specific agents to block individual transporter proteins. These substances can thus be used to selectively influence the exchange of substances in the body.

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 3,000 employees is the largest biomedical research institute in Germany. At DKFZ, more than 1,000 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. Jointly with Heidelberg University Hospital, DKFZ has established the National Center for Tumor Diseases (NCT) Heidelberg, where promising approaches from cancer research are translated into the clinic. In the German Consortium for Translational

Cancer Research (DKTK), one of six German Centers for Health Research, DKFZ maintains translational centers at seven university partnering sites. Combining excellent university hospitals with high-profile research at a Helmholtz Center is an important contribution to improving the chances of cancer patients. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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