

## **Peptide acts as mediator for learning**

**In order to adapt to changes in the environment, the brain produces new nerve cells (neurons) even at adult age. These young neurons are crucial for memory formation and learning. Scientists from the German Cancer Research Center (DKFZ) and Heidelberg University Hospital have now discovered that a small peptide plays the role of a mediator in this process. In response to an external stimulus such as a varied environment, the mediator peptide boosts the proliferation of neural stem cells and neural progenitor cells.**

The ability of the brain to respond and adapt to changes is scientifically called brain plasticity. This ability is the basis of all learning processes. New neurons, which can still be generated in the adult brain in specific areas, are instrumental in this process.

“But until now it has been unknown which molecular processes translate environmental changes into the production of new neurons,” said Hannah Monyer, who leads the Cooperational Division of Clinical Neurobiology of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and Heidelberg University Hospital. “In our current study, we have found a key mediator in this process for the first time.”

Monyer and her team have revealed in their current study that a small peptide called DBI (short for: diazepam binding inhibitor) is the crucial mediator in this process. The peptide was first identified because it binds to the receptor for a chemical messenger in the brain called GABA, where it replaces a drug called Diazepam (Valium).

Recently, Monyer and colleagues already reported that DBI promotes the development of new neurons in an area of the brain called subventricular zone. This brain area is responsible for the supply of new nerve cells in the olfactory system, which is particularly sophisticated in rodents. In her present work, the Heidelberg neuroscientist shows that DBI has the same function in the hippocampus – the portion of the brain where memory formation and learning are located.

New neurons that form in the hippocampus improve orientation and learning capacity in the animals. Numerous research studies have already provided proof that in mice physical activity or variations in their environment stimulate neurogenesis in the hippocampus.

The researchers in Monyer’s team used various genetic methods to turn off the DBI gene in this brain region in mice or, alternatively, to strongly boost it. When DBI was absent, the numbers of neural stem cells in the hippocampus declined. An oversupply of the peptide caused the opposite to happen, i.e., the investigators found more neural stem and progenitor cells.

Equipping the cages with toys is an established method to stimulate the generation of new neurons in the hippocampus in rodents. However, in mice whose DBI gene had been silenced using molecular-biological tricks, the stimulating environment failed to have an effect: The quantities of neural stem cells could not be increased.

DBI exerts its effect by binding to the receptor for the chemical messenger GABA in the neural stem cells, thus acting as a molecular antagonist of this neurotransmitter. “GABA is responsible for keeping the stem cells dormant in their niche without dividing,” explained Monyer. “When

DBI enters the scene, they start proliferating, thus enlarging the stem cell pool that is available as a reservoir for young neurons. In DBI, we seem to have found the key mediator. The peptide suppresses the effect of GABA and thus links the environmental stimuli to the production of new neurons that are required for learning.”

Ionut Dumitru, Angela Neitz, Julieta Alfonso and Hannah Monyer: Diazepam Binding Inhibitor Promotes Stem Cell Expansion Controlling Environment-Dependent Neurogenesis. Neuron 2017, DOI: 10.1016/j.neuron.2017.03.003

An image for this press release is available at:

<http://www.dkfz.de/de/presse/pressemitteilungen/2017/bilder/Dumitru-et-al.jpg>

Caption: Generation of new neurons in the hippocampus of mice. DBI (Diazepam binding inhibitor) is dyed red, the two stem cell markers nestin and SOX2 are dyed green and cyan, respectively.

**Note on use of images related to press releases**

Use is free of charge. The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) permits one-time use in the context of reporting about the topic covered in the press release. Images have to be cited as follows: “Source: Ionut Dumitru, DKFZ”.

Distribution of images to third parties is not permitted unless prior consent has been obtained from DKFZ’s Press Office (phone: ++49-(0)6221 42 2854, E-mail: [presse@dkfz.de](mailto:presse@dkfz.de)). Any commercial use is prohibited.

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.

**Contact:**

Dr. Stefanie Seltsmann  
Head of Press and Public Relations  
German Cancer Research Center  
Im Neuenheimer Feld 280  
D-69120 Heidelberg  
T: +49 6221 42 2854  
F: +49 6221 42 2968  
[presse@dkfz.de](mailto:presse@dkfz.de)

Dr. Sibylle Kohlstädt  
Press and Public Relations  
German Cancer Research Center  
Im Neuenheimer Feld 280  
D-69120 Heidelberg  
T: +49 6221 42 2843  
F: +49 6221 42 2968  
Email: [presse@dkfz.de](mailto:presse@dkfz.de)