No. 20 April 6, 2017 (Koh)

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.

Contact:

Dr. Stefanie Seltmann
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

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