Lack of coronin 1 protein causes learning deficits and aggressive behavior

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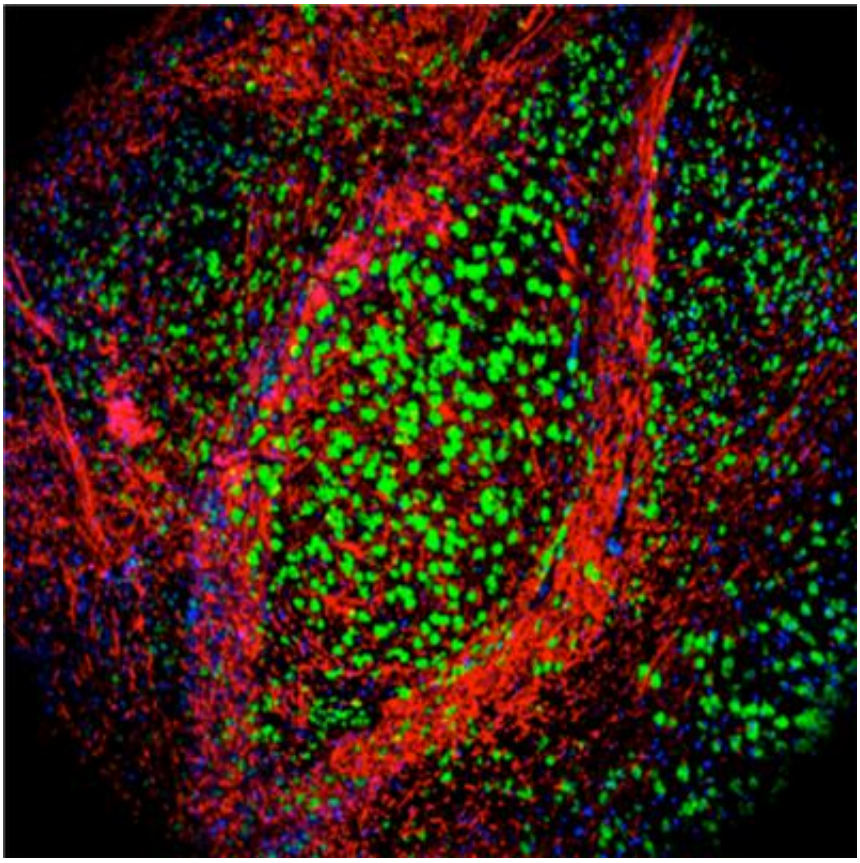

The absence of coronin 1 in neurons results in severe neurobehavioral defects. Coronin 1 (green) in neurons within the amygdala of the brain. Red: neurofilament as neuronal marker; Blue: nuclear stain. Credit: University of Basel, Biozentrum

Learning and memory relies on the proper processing of signals that

stimulate neuronal cells within the brain. Researchers at the Biozentrum of the University of Basel, together with an international team of scientists, has uncovered an important role for the protein coronin 1 in cognition and behavior. They found that a lack of coronin 1 in mouse and in man is associated with poor memory, defective learning and aggressive behavior. The results, recently published in *PLOS Biology*, identify a novel risk factor for neurobehavioral dysfunction and reveal a molecular pathway involved in transferring information within neurons.

Organisms must be able to sense signals from the outside and translate these into biochemical cues in order to adequately respond to their environment. This capability is also required to process information that reaches the brain. Within the brain, stimulation of neurons activates genes that are required, for example for learning and memory. In collaboration with an international and interdisciplinary team the research group led by Prof. Jean Pieters from the Biozentrum, University of Basel, has now uncovered the role of an evolutionarily conserved protein, called coronin 1, in providing a link between the extracellular stimulus and neuronal activation that ultimately results in efficient learning and memory in both mice and men.

From the immune system to the brain

In earlier work, Pieters' team discovered the protein coronin 1 as being essential for the proper transduction of signals in immune cells. In mice lacking coronin 1 the researchers further investigated the molecular mechanism. Surprisingly, these mice showed aberrant behavior. In particular, mice lacking coronin 1 appeared to be far more aggressive and display extreme grooming activity, an indication of reduced sociability. An in-depth analysis in collaboration with scientists from the Friedrich Miescher Institute in Basel and the University of Bordeaux unveiled profound learning and behavioral problems and severe defects in the ability to activate neurons in the absence of coronin 1.

Activation of a signaling cascade

But how does coronin 1 ensure proper neurobehavioral functioning? Normally, stimulation of the cell surface results in an activation of an intracellular cascade of reactions and ultimately stimulates the production of the signaling molecule cAMP which then activates a number of processes, including the transcription of gene involved in neurobehavior. "We found that in the absence of coronin 1, cell surface stimulation leads to a defective cAMP production", explains Pieters. "This in turn affects the signal transduction which is finally responsible for the deficits in learning and memory formation."

Of mice and men

Furthermore, the researchers analyzed the clinical history of a patient lacking coronin 1 due to a mutation: it turned out that this patient showed learning defects and aggressive behavior. With this study, Pieters and his project collaborators not only define a crucial role for coronin 1 in cognition and behavior, but also unravel a coronin 1-dependent signaling pathway that may be explored both for potential risk factors as well as future interventions to modulate neurobehavioral dysfunction.

More information: Rajesh Jayachandran, Xiaolong Liu, Somdeb BoseDasgupta, Philipp Müller, Chun-Lei Zhang, Despina Moshous, Vera Studer, Jacques Schneider, Christel Genoud, Catherine Fassoud, Fréderic Gambino, Malik Khelfaoui, Christian Müller, Deborah Bartholdi, Helene Rossez, Michael Stiess, Xander Houbaert, Rolf Jaussi, Daniel Frey, Richard A. Kammerer, Xavier Deupi, Jean-Pierre de Villartay, Andreas Lüthi, Yann Humeau, and Jean Pieters. "Coronin 1 Regulates Cognition and Behavior through Modulation of cAMP/Protein Kinase A Signaling." *PLOS Biology*, published March 25, 2014 | DOI: 10.1371/journal.pbio.1001820

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