

DREAM: One gene regulates pain, learning and memory

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The DREAM-gene which is crucial in regulating pain perception seems to also influence learning and memory. This is the result of studies carried out by researchers in Seville, Spain, and Vienna, Austria. The new findings could help explain the mechanisms of Alzheimer's disease and yield a potential new therapeutic target.

In 2002, a group of scientists at the University of Toronto was able to identify a gene which they dubbed DREAM (downstream regulatory element antagonistic modulator). The gene's function was highly interesting: it obviously served as a key regulator in the perception of pain. Mice who lacked the gene showed clear signs of markedly reduced sensitivity to all kinds of pain, whether chronic or acute. Otherwise, the mice appeared perfectly normal.

The work leading to these findings was carried out in the lab of Josef Penninger, then principal investigator at the Amgen Institute in Toronto. The publication describing the gene's function was received with great interest (*Cell*, Vol. 108, 31-43, 11.1.2002) and DREAM was subsequently termed the "Master-Gene of pain perception".

Josef Penninger, meanwhile scientific director of IMBA, the Institute of Molecular Biotechnology of the Austrian Academy of Sciences in Vienna, continued to wonder what other surprises DREAM might have in store. In a collaborative effort with neurobiologists from the University Pablo de Olivade (Seville) he devised experiments to follow up on the previous findings. A team of scientists under Ángel Manuel

Carrión subjected DREAM-less mice to numerous neurological tests and analyzed their memory skills. The results were striking: without DREAM, mice were able to learn faster and remember better. Fascinatingly, the brains of aged mice (18 months) showed learning capacities similar to those of very young mice.

Thus, DREAM turns out to be a genetic candidate for explaining old age dementia. Even a causal connection to Alzheimer's disease seems plausible. Studies published in mid 2008 suggest that the devastating condition may be related to Calcium regulation gone awry. The accumulation of amyloid plaques in brain cells, usually blamed for Alzheimer's, might be a consequence of the Calcium-imbalance rather than the culprit for the disease.

Calcium regulation is also responsible for tuning the activity of the DREAM-gene. Calcium homeostasis may thus be the link between pain perception, learning and memory. This is supported by observations of patients suffering from chronic pain: very often their ability to memorize is strikingly reduced and they need a lot more time to learn than individuals without pain.

"It is absolutely fascinating that we found a gene which at the same time regulates pain, learning and old age memory function", says Josef Penninger, "and it is of great interest to the millions of people suffering from chronic pain that we follow up on these results."

More information: The paper „Lack of DREAM protein enhances learning and memory and slows brain aging" by Fontán-Lozano et al. has been published in the current issue of the *Journal Current Biology* [Curr Biol. 2009 Jan 13;19(1):54-60].

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