IMBA Press Release

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Institute of Molecular Biotechnology
of the Austrian Academy of Sciences

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Institute of Molecular Biotechnology
Dr. Bohr-Gasse 3, 1030 Vienna, Austria
Tel: +43-1-790 44
Fax: +43-1-790 44/110
www.imba.oeaw.ac.at

Contact:
Dr Heidemarie Hurtl
tel. +43 1 79730/3625
mobile: +43 664 8247910
heidemarie.hurtl@imba.oeaw.ac.at

Scientific Contact:
Prof Josef Penninger, Director
tel. +43 1 79730/4702
josef.penninger@imba.oeaw.ac.at

Pain gene found in flies, mice and people may have links to creativity

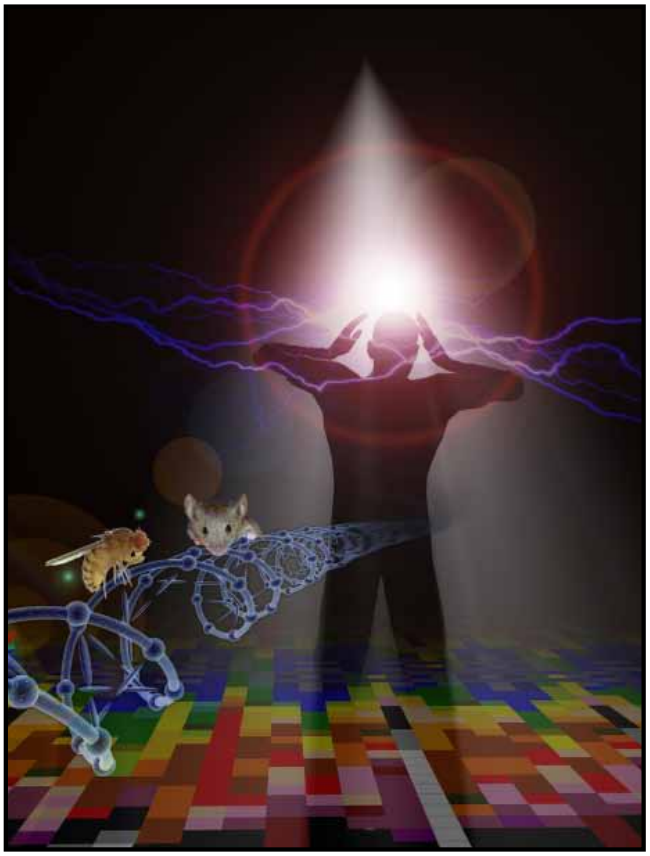
A newly discovered gene which helps to control the sense of pain is linked to synaesthesia, when sensations such as touch also affect other senses like hearing or sight. The rare condition causes some people to see sounds or written words as colours, or experience tastes, smells and shapes in linked combinations. Famous synaesthetes include composers Franz Liszt or Olivier Messiaens, and this condition has been linked to creativity and intelligence.

Now Austrian medical researchers have identified a gene variation which reduces the sense of pain, giving hope for future treatments of pain sufferers, according to new research published in the journal Cell today (12 November 2010). Around one in five people around the world suffer from acute or chronic pain, with all its financial costs and emotional burden. Studies of twins have shown that at least half of the differences in the way we are sensitive to pain is inherited.

Scientists at the Institute of Molecular Biotechnology of the Austrian Academy of Sciences in Vienna, led by Josef Penninger and Greg Neely, together with Clifford Woolf of Harvard Medical School, Boston, developed a system in fruit flies to model pain perception. The system allowed them to screen nearly the entire set of the fly's genes in search for those that affect the insect's response to noxious heat. After identifying 600 pain genes the researchers closed in on one known as α2δ3 which is involved in calcium ion channels. Doctors already know that these tiny pores in the cell membrane are targeted by some existing analgesics, helping to relieve pain, so it seemed a promising candidate gene for further studies.

The next stage was to test whether the α2δ3 gene also affects the way people feel heat and pain. Doctors in the USA looked at four different single-letter variations in DNA, within or close to the α2δ3 gene in 189 healthy volunteers. They found that some of the gene variations led to reduced sensitivity to acute pain in a test which gives the volunteer a quick series of heat pulses. Further testing in 169 patients who had undergone surgery for back pain caused by damaged discs showed that patients with these same gene variations were much less likely to have persisting chronic pain.

The research team then looked directly into the brain of mice with mutant α2δ3 genes with MRI scanners and, in cooperation with the group of Andreas Hess in Erlangen, Germany, showed that this gene controls the way heat pain signals are processed in the brain. In the mutant mice the nerve signals arrive in the brain correctly at the thalamus, a first pain processing centre, but are not



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properly sent on to the higher processing centres in the cortex, which should alert the animals to the sensation of pain. Instead the researchers found that areas in the brain cortex for sight, smell and hearing were being activated by the pain signal. Thus, the team stumbled upon the first ever known gene that appears to control sensory cross-activation or synaesthesia - a neurological condition where a stimulus of one sense triggers perception of another sense.

“To find that our mice showed sensory cross-activation was the most stunning result of our study, it was something we never looked for”, says Josef Penninger. “Multiple forms of synaesthesia exist including pain stimuli that trigger colour. Synaesthesia might affect up to 4% of the population, shows genetic linkage, and has been associated with intelligence and creativity. Thus, α2δ3 mutant mice might provide the first ever animal model to enable us to study the phenomenon of sensory cross-activation. This might open up an entirely new field of biology.”

“Genes give us an amazing and powerful tool to begin to understand how pain is generated, and which functional pathways and specific proteins are involved”, says Dr Woolf. “Understanding the molecular basis of pain will lead to the development of new analgesics, the identification of risk factors for chronic pain and improved decision-making about the suitability of surgical treatment for different patients”.

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The paper „A genome-wide Drosophila screen for heat nociception identifies α2δ3 as an evolutionary conserved pain gene” (Neely et al.) will be published in Cell on November 12, 2010.

The IMBA – Institute for Molecular Biotechnology of the Austrian Academy of Sciences opened in 2003. It combines fundamental and applied research in the field of biomedicine. Interdisciplinary research groups address functional genetic questions, particularly those related to the origin of disease. The ultimate goal is to implement acquired knowledge into the development of innovative applications for prevention, diagnosis and treatment of disease.

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