UNIVERSITÉ DE GENÈVE

PRESS RELEASE

Geneva | 30 July 2012

under embargo until Thursday 2 August 2012, 6pm, Swiss time

Sexual harassment and abuse: when genetics get involved

Researchers from the University of Geneva, Switzerland, decipher the molecular basis of the female mouse nuptial parade, as well as an atypical form of aggression linked to a mutation

Frontiers in Genetics
National Center of Competence in Research
Nationaler Forschungsschwerpunkt
Pôle de Recherche National

The courtship period in mice displays surprising rituals. Researchers from the University of Geneva (UNIGE) show, indeed, that the female actively solicits the male's advances, as well as mating. They also demonstrate that this courtship activity is under genetic control, as evidenced by the aggressive behavior of females issued from a mutant line. The latter chase the males and investigate their intimate parts relentlessly, before inflicting them genital bites. This behavior is associated with the deletion of a specific region in a group of genes named *HoxD*. The anomaly induces in mutant female brain ectopic expression of the *Hoxd10* gene. The results, published in the journal *Current Biology*, open new avenues to explore genetic and molecular bases of normal and pathological mammalian affect.

The 'architect genes' orchestrating the mammalian's construction body plan have been trailed for the past two decades by Denis Duboule, professor at the UNIGE and the Ecole polytechnique fédérale de Lausanne, Switzerland. For this purpose, his group has created various mutant mice lines. One of them, which harbors a deletion within a cluster of architect genes named *HoxD,* displays unprecedented behavior. 'Females carrying this mutation behave normally, except during sexual receptivity. At that moment, however, they pursue males ruthlessly, with increased investigation and biting of their genitals', says Jozsef Zakany, researcher at the Department of Genetics and Evolution of the UNIGE.

An extreme deviation from the norm

This uncontrolled and severely exacerbated activity is accompanied by tactile stimulation directed at the genitals, alternating with sexual intercourses. While all of the males are pursued in the same way, other females are never subjected to this behavior. 'As to the males, they never react aggressively, even after mutilation of their genital region', notes with surprise Denis Duboule, director of the NCCR *Frontiers in Genetics* program.

The compulsive sexual solicitation, which was hitherto unreported and fits no known pathological behavior in rodents, is observed only in females. It is transmitted to their progeny by a dominant allele (a variant of a gene) that the authors named *'Atypical female courtship'*, abbreviated $HoxD^{Afc}$.

What is the link between a deletion of a precise region in the *HoxD* gene cluster and a behavior amounting to aggravated sexual harassment? To answer this question, the biologists have looked for differences in mutated mice, in particular within the brain. 'We found out that the *Hoxd10* gene, which is adjacent to the deletion, is ectopically

expressed in the forebrain, mainly in the hippocampus', reports Jozsef Zakany.

A defective behavioral inhibition system

Hox genes, which encode transcription factors, are believed to have no function in the forebrain. The protein encoded by *Hoxd10* in certain cells of the hippocampus may thus trigger important changes in the implementation of their genetic program, in particular during the pre-ovulatory phase. In this case, the protein may impinge upon the capacity of these cells to modulate behavioral sexual responses.

Although anomalies linked to various mutations in the *HoxD* gene cluster have been documented in humans, none has been reported in relation with deviant sexual behavior. 'The pathological pattern we report rather evokes human conditions like complex psychomotor temporal lobe epilepsy or Kluver Bucy syndrome', explains Denis Duboule.

The unknown words of rodents' love language

This study has also brought the discovery of the normal nuptial parade of female mice. Contrary to popular belief, it is the female that initiates sexual approach and mating, by an active solicitation of the male's advances. Unveiling the genetic control of this activity opens new avenues to study the molecular bases of normal and pathological mammalian affect.

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