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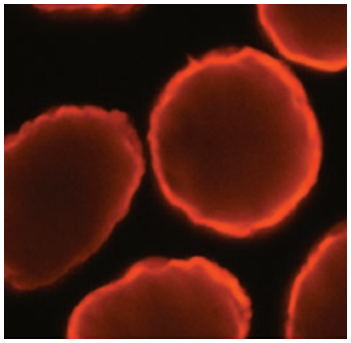
DEVELOPMENTAL BIOLOGY

Testicular eggs show role of early genomic imprinting

Development of immature germ cells into sperm or eggs is mainly determined by sex chromosomes, XX for female and XY for male. Previous studies suggest that the body's environment can also direct germ cell differentiation. To determine how the environment of the testes impacts germ cell development, Ayako Isotani *et al.* fused female and male embryos to create XX–XY chimeric embryos containing both female and male cells. One X chromosome of the female cells was labeled with GFP to track cellular development in the testes. The researchers observed that most female germ cells developed into sperm progenitor cells, demonstrating that the cells underwent paternal imprinting despite their chromosomal makeup. On the other hand, a small number of female germ cells developed into "testicular eggs" that formed zona pellucida and could fuse with sperm, but these eggs, when fertilized, were not able to develop into embryos. Isotani *et al.* hypothesize that early molecular events initiated egg formation in these cells via maternal imprinting, which could not be overridden by the testicular environment. These results indicate that germ cell differentiation is not always determined by chromosomes or environmental conditions, but may be defined by the sex that was chosen by the germ cells during early embryonic stages of development.



Zona pellucida of testicular eggs.

"Genomic imprinting of XX spermatogonia and XX oocytes recovered from XX↔XY chimeric testes" by Ayako Isotani, Tomoko Nakanishi, Shin Kobayashi, Jiyoung Lee, Shinichiro Chuma, Norio Nakatsuji, Fumitoshi Ishino, and Masaru Okabe (see pages 4039–4044)

EVOLUTION

Harmful but mild silent mutations among humans and chimps

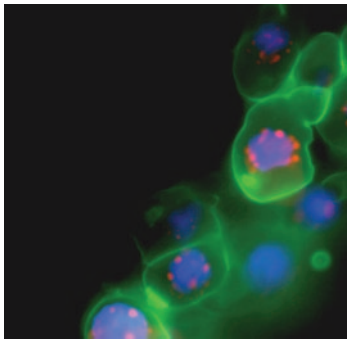
Nearly all of the silent mutations between human and chimpanzee genomes are harmful to either species, researchers report, but they are so mildly harmful that they have escaped being weeded out by natural selection. The role of weak selection, which is weaker than genetic drift, has been debated by scientists in recent decades, but the task of measuring the strength of such selection is particularly difficult. Jian Lu and Chung-I Wu used genomic data from chimpanzees and humans to compare the rate at which genes from these species have evolved over time. The authors looked specifically at synonymous substitutions between the two genomes, which change the rate at which a protein is made but do not change the type of protein itself. The authors found that synonymous substitutions on the X chromosome of humans and chimpanzees were less frequent than those on the autosomes. Lu and Wu also reported that at least 90% of the synonymous substitutions between humans and chimpanzees were deleterious. On the other hand, X-linked nonsynonymous substitutions were ≈30% more frequent than autosomal ones, suggesting the fixation of advantageous but recessive mutations. How evolution permitted so many deleterious silent mutations to accumulate raises many questions and may reveal the mechanism of selection on the rate of protein synthesis. The authors speculate that a few strong advantageous mutations might have been enough to compensate for the associated, diffuse deleterious mutations.

"Weak selection revealed by the whole-genome comparison of the X chromosome and autosomes of human and chimpanzee" by Jian Lu and Chung-I Wu (see pages 4063–4067)

GENETICS

Switching off the feminizing touch

Primordial germ cells (PGCs), which eventually develop into either sperm or eggs, play an unanticipated role in zebrafish sex



Zebrafish primordial germ cells.

determination, according to Krasimir Slanchev *et al*. Although an ovary-like structure is initially formed in all zebrafish embryos, the authors showed that ablating PGCs led embryos to develop into sterile males. Slanchev *et al.* used two methods to ablate the PGCs. In the first experiment, *dead end* antisense oligonucleotides eliminated the germ-line cells; *dead end* is essential for normal migration and survival of PGCs. All embryos treated with this oligonucleotide developed into males with shape and color resembling wild type and with normal sexual behavior, i.e., inducing females to lay eggs. The second system preferentially expressed a toxic protein called Kid in the PGCs and the antidote Kis protein throughout somatic tissues. The researchers found that the gonads degenerated in absence of PGCs. In experimental embryos lacking these cells, the gonad structure is smaller and uniform 35 days after fertilization compared with controls, in which the oocyte-laden ovaries or testes had developed. At 90 days after fertilization, no gonad structures were visible. Thus, the authors hypothesize that the loss of PGCs leads to the decline of gonadal tissue, which, in turn, decreases the conversion of testosterone to estrogen, eliminating the feminizing touch.

"Development without germ cells: The role of the germ line in zebrafish sex differentiation" by Krasimir Slanchev, Jürg Stebler, Guillermo de la Cueva-Méndez, and Erez Raz (see pages 4074–4079)

NEUROSCIENCE

Cocaine addiction and metabotropic glutamate receptor

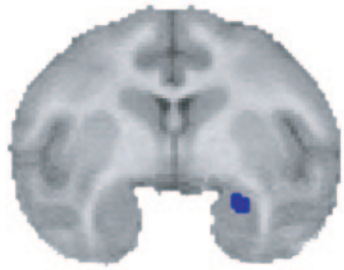
Group 2 metabotropic glutamate receptors (mGluRs) have been associated with disorders such as Parkinson's disease and anxiety, but their physiological role in brain function is poorly understood. To explore this role, Yosuke Morishima *et al.* studied the behavior of mGluR2 knockout mice. The authors found that the mice behaved normally under general observation but showed abnormalities under various types of enforced situations. After repeated cocaine administration, the knockout mice showed greater hyperactivity and greater conditioned place preference compared with wild-type mice, both of which are signs of increased addiction. Morishima *et al.* also showed that the mice were hyperactive in new environments and stressful situations and had impaired motor coordination in tests of balance. Extracellular levels of dopamine in the nucleus accumbens of the knockout mice increased with cocaine administration, and the response pattern of glutamate release changed. The results suggest that the inhibitory mGluR2 plays a pivotal role in synaptic regulation of glutamatergic transmission in the neural network.

"Enhanced cocaine responsiveness and impaired motor coordination in metabotropic glutamate receptor subtype 2 knockout mice" by Yosuke Morishima, Tsuyoshi Miyakawa, Tomoyuki Furuyashiki, Yasuhiro Tanaka, Hiroshi Mizuma, and Shigetada Nakanishi (see pages 4170–4175)

NEUROSCIENCE

Monkeys' cries for help related to two brain systems

When distressed primates cry out to their social groups for help, the intensity of their cries may be related to the balance of their perception of threat and their drive for affiliation, researchers report. Calling for help during times of separation is vital but risky behavior; vocal cries can alert not only other group members but predators as well. Although this behavior is universal in primates, little is known about the neural circuitry that underlies individual differences in calling for help. Andrew Fox *et al.* observed 25 rhesus monkeys separated from their cage mates and noted the frequency of the monkeys' coo calls. The authors examined metabolic activity in the monkeys' brains by high-resolution positron-emission tomography scanning. Fox *et al.* showed that the frequency of a monkey's cries for help was related to changes in two areas of the brain: increased activity in the right dorsolateral prefrontal cortex, which mediates goal-directed behavior, and decreased activity in the amygdala, which mediates threat detection. Taken together, these two regions accounted for 76% of the variance of the monkeys' calls for help. These findings in monkeys are relevant to humans and provide a conceptual neural framework to understand why and how individuals behave when finding themselves in need of social support.



Amygdala correlates with monkey cooing frequency.

"Calling for help is independently modulated by brain systems underlying goal-directed behavior and threat perception" by Andrew S. Fox, Terrence R. Oakes, Steven E. Shelton, Alexander K. Converse, Richard J. Davidson, and Ned H. Kalin (see pages 4176–4179)