Biology

Endogenous Non-retroviral RNA Virus Elements in Mammalian Genomes

This paper shows the first evidence for endogenization of non-retroviral RNA virus in mammalian species. We discovered the elements homologous to the nucleoprotein (N) gene of bornavirus, a non-segmented, negative strand RNA virus, in the genomes of several mammals including humans, non-human primates, rodents and elephants. We also demonstrated that N mRNA of a bornavirus, Borna disease virus (BDV), is reverse-transcribed and integrated into the genome DNA of persistently infected cells, although BDV does not encode reverse transcriptase. Our findings provide novel insights not only into generation of endogenous elements of RNA viruses but also into a role of bornavirus as a source of genetic novelty in its host.

Browinan Search-and-catch Mechanism for Myosin-VI Steps
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Myosin-VI is a two-legged cargo transporter that “walks” along an actin filament in cells. During walking motion, myosin leg undergoes Brownian motion, resulting in a “drunkenly walking”. A key question is how the Brownian leg searches for and catches the forward actin target. Here, we developed a rapid (microsecond) mechanical manipulation technique using optical tweezers and applied force to the single Browanian leg. We found the strongly catch in the forward actin is accelerated by the mechanical strain. We propose the strain-dependent asymmetric catch mechanism is the origin of the rectification of the Brownian motion and would be useful for efficient and adaptable walking in the cell.

The widespread existence of large cis-regulatory regions is a remarkable feature of mammalian genomes and potentially involved in the etiology of human genomic disorders. Characterization of such regions, however, has been hampered by the limited availability of tools for manipulating large genomic regions in model animals. Here we propose a novel experimental approach using targeted integration of the Sleeping Beauty transposon into the mouse genome. The “local hopping” capability of the transposon allowed scanning of the surrounding genomic region with a reporter gene cassette, revealing the location and territory of enhancer actions along the chromosome.

Protein Kinase G Dynamically Modulates TASK1-Mediated Leak K+ Currents in Cholinergic Neurons of the Basal Forebrain
Toyoda, H.; Saito, M.; Okazawa, M.; Abe, H.; Takada, K.; Funabiki, K.; Takada, M.; Kaneo, T.; Kang, Y. (Graduate School of Dentistry) (Graduate School of Frontier Biosciences)

Leak K+ conductance generated by TASK1/3 inhibition respectively up- and down-regulates TASK1 channels heterologously expressed in PKG-loaded HEK293 cells at physiological pH, by shifting the pH-sensitivity of TASK1 channels in the acidic and basic directions, respectively. In the cholinergic basal forebrain (BF) neurons, similar modulations of TASK1-like pH-sensitivity of leak K+ currents were caused by PKG. It is strongly suggested that PKG activation and inhibition dynamically modulates TASK1 currents at physiological pH by bidirectionally changing K+ values for protonation of extracellular pH-sensors of TASK1 channels in cholinergic BF neurons.

Protocadherin-11 family is required for serotonergic projections to appropriately innervate target brain areas.

Serotonergic neurons play a pivotal role in psychiatric disorders such as depression. Serotonergic neurons in the brainstem project their axons to every region of the brain. However, this molecular mechanism had been almost unknown. We found that protocadherin-11 genes, encoding transmembrane proteins, were strongly expressed in serotonergic neurons, and that in protocadherin-11 mutant mice serotonergic axons were abnormally clumped in the areas proximal to the final target brain areas such as the hippocampus (see the figure). This result demonstrates that protocadherin-11 proteins regulate the distribution of serotonergic axon terminals.

We assessed the effects of the induction of immature status-related genes and showed the introduction of induced pluripotent stem cells with retroviral-mediated methods in gastrointestinal cancer cells. The pluripotency was represented in the induced cells, and the induced pluripotent cancer (iPC) cells were remarkably distinct from parental cancer cells. To determine the differentiation ability, iPC cells were grown in differentiation-stimulating culture condition. These cultured cells, termed post-iPC cells, showed slow proliferation and were sensitized to chemotherapy and differentiation-inducing reagents in vitro. In vivo analysis showed that tumorgenesis was reduced. These results demonstrated the novel cancer treatment in addition to the conventional therapy, and the exploitation of drug producing strategy towards future clinical applications.

A Transposon-Based Chromosomal Engineering Method to Survey a Large Co-regulatory Landscape in Mice.
Kokubu C.; Hori, H.; Abe, K.; Reda R.; Mizuno S.; Uno K.; Ogawa S.; Oohua M.; Iwane, H. A. (Graduate School of Medicine) (Graduate School of Medicine) (Graduate School of Dentistry) (Graduate School of Medicine)

The EMBO Journal, 29, 1192-1204 (2010)

A 1-Megadalton Translocation Complex Containing Tic20 and Tic21 Mediates Chloroplast Protein Import at the Inner Envelope Membrane

The Plant Cell, 21, 1781-1797 (2009)

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Defined factors induce reprogramming of gastrointestinal cancer cells