This Week in The Journal

● Cellular/Molecular

Spontaneous Astrocytic Ca^{2+} Oscillations and Neurite Growth

Kazunori Kanemaru, Yohei Okubo, Kenzo Hirose, and Masamitsu Iino

(see pages 8957-8966)

This week, Kanemaru et al. explore the signaling pathway between spontaneous Ca^{2+} oscillations in cultured astrocytes and the promotion of neurite growth. Their results reveal a role for the membrane-bound adhesion molecule N-cadherin. The authors blocked Ca^{2+} oscillations by preventing IP_3 signaling with retroviral-mediated expression of IP_3 5-phosphatase (5ppase). This molecule hydrolyzes IP_3 and thus prevented spontaneous astrocytic Ca^{2+} oscillations. Growth cone motility was compromised in hippocampal neurons cultured with 5ppase-expressing astrocytes. Interference with neurotransmitter-evoked astrocytic Ca^{2+} transients did not affect neurite outgrowth. The messenger was not diffusible because direct contact with an astrocyte deficient in spontaneous Ca^{2+} signaling arrested growth cone advancement. Surface expression of the growth-promoting molecule N-cadherin was downregulated in 5ppase-expressing astrocytes, and neuronal growth cone advancement was rescued by extrinsic expression of N-cadherin on astrocytes.

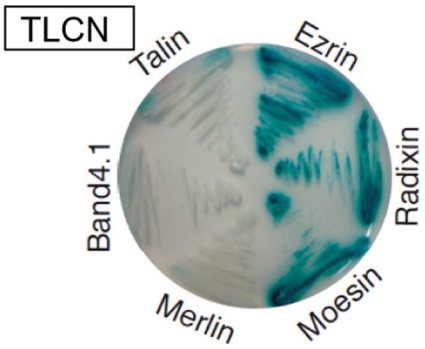
▲ Development/Plasticity/Repair

Forming Filopodia

Yutaka Furutani, Hitomi Matsuno, Miwa Kawasaki, Takehiko Sasaki, Kensaku Mori, and Yoshihiro Yoshihara

(see pages 8866-8876)

Before synapses form between axons and dendrites, even before dendritic spines take shape, dendritic filopodia are out there, poking and prodding and exploring their surroundings. In this week's *Journal*, Furutani et al. searched for intracellular binding partners for telencephalin (TLCN), a telencephalon- and dendrite-specific cell adhesion molecule that is expressed in filopodia. A yeast two-hybrid screen revealed interactions with ezrin, radixin, and moesin of the so-called ERM family; these adaptors link membrane proteins to the actin cytoskeleton. The binding of the cytoplasmic domain of TLCN to ERMs was confirmed using surface plasmon resonance analysis of direct protein–protein interactions. Phosphorylated ERM proteins colocalized with TLCN in filopodia, but not spines, and contributed to filopodial formation. Reduction of ERM protein expression by small interfering RNA decreased the density and length of filopodia while accelerating spine maturation, whereas ectopic expression of constitutively active ezrin induced the formation of dendritic filopodia.



A β-galactosidase (LacZ) reporter (blue) in yeast was used to assess protein interactions between TLCN and the ERM proteins ezrin, radixin, and moesin. See the article by Furutani et al. for details.

■ Behavioral/Systems/Cognitive

Kisspeptin–GPR54 Signaling in Sexual Differentiation

Alexander S. Kauffman, Jin Ho Park, Anika A. McPhie-Lalmansingh, Michelle L. Gottsch, Cristian Bodo, John G. Hohmann, Maria N. Pavlova, Alex D. Rohde, Donald K. Clifton, Robert A. Steiner, and Emilie F. Rissman

(see pages 8826 – 8835)

Long before their role during puberty and adulthood becomes manifest, gonadal hormones exert influence on the development of sexual dimorphism in the brain. This week, Kauffman et al. examined the role of GPR54, a G-protein-coupled membrane receptor for kisspeptin, in the development of sexually dimorphic traits. Gonadotropin-releasing hormone (GnRH) neurons were activated and released leutinizing hormone after treatment with kisspeptin in wild-type male mice but not in mice lacking *GPR54*. *GPR54*-deficient males showed the expected male sexual behavior after treatment with testosterone, but they lacked preference for estrous females on olfactory-mediated partner preference behavior. In the anteroventral periventricular nucleus, a sexually dimorphic structure where there are more tyrosine hydroxylase- and Kiss1-expressing neurons in females than males, *GPR54*-deficient males had a female phenotype. They also had reduced motoneurons in the spinal nucleus of the bulbocavernosus, another sexually dimorphic structure. Thus, kisspeptin–GPR54 signaling is required for sexually dimorphic development but not for sexual behavior per se.

♦ Neurobiology of Disease

Mapping the Regulation of Negative Moods

Tom Johnstone, Carien M. van Reekum, Heather L. Urry, Ned H. Kalin, and Richard J. Davidson

(see pages 8877– 8884)

This week, Johnstone et al. take the position that everyone has blue moods, but the failure to effectively regulate those moods might underlie susceptibility to major depressive disorder. The authors used functional magnetic resonance imaging to map the patterns of brain activation in depressed and nondepressed subjects as they viewed a standard set of emotionally positive or negative pictures. In order to decrease the associated emotion, subjects were instructed to imagine, for example, a happy outcome for a negative image. Pupil dilation provided a measure of arousal. During the reappraisal, nondepressed subjects showed increased activity in the left prefrontal cortex (PFC), whereas depressed subjects showed bilateral increases, indicating greater recruitment of right PFC in the depressed subjects. Control subjects with the highest ventromedial prefrontal cortex (VMPFC) activation during reappraisal showed less activation in the amygdala, whereas amygdalar activation increased with greater VMPFC activity in depressed subjects.