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EDITORIAL

In focus in HCB

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New system for monitoring brain neuronal activity in moving rats

One of the great challenges in live animal imaging is the accurate recording of brain neuronal activity in a free-moving animal. Although multiphoton confocal microscopy has been used successfully to image more peripheral regions of the brain (Kerr et al. 2005), deeper regions remain inaccessible. Iijima et al. (2017) have now developed a system consisting of (1) a single optical fiber for recording neuronal activity via eGFP expression (linked to gonadotropin releasing hormone), and (2) a newly designed animal cage whereby the floor rotates in response to head movements, thus minimizing animal movement-derived stress on the optical fiber, for monitoring and imaging via fluorescence structures deep in the brain. This system allowed real-time fluorescence monitoring in awake and active animals over several days. By replacing the animal's water with a mild saline solution (to induce dehydration), they found an increase in eGFP fluorescence intensity in the paraventricular nucleus region. To refine their system to allow recording from individual neurons, the authors replaced the original optical fiber with a bundle containing approximately 3000 thin optical fibers and connected to an upright fluorescence microscope. Using this higher resolution system, they imaged eGFP expressing neurons in the hypothalamus of active rats over many hours. This newly developed system thus offers a novel means to monitor and image fluorescently labeled neurons in deep regions of an awake and active rat.

Rotenone effect on peroxisomal dynamics mediated by microtubules

Redox biology is an area of great interest for cell biological responses in health and disease (Little et al. 2017). Two major cellular organelles involved in reactive oxygen species (ROS) signaling are mitochondria and peroxisomes. Like many intracellular organelles, these organelles are also known to interact dynamically with one another in what is referred to as the "peroxisome–mitochondria connection" (Schrader et al. 2015). Although effects of the generation of oxidative stress in peroxisomes on mitochondrial function and morphology are well known, very little is known concerning potential effects of mitochondrial-derived oxidative stress on peroxisomal structure or function. To address this issue, Passmore et al. (2017) have performed experiments to examine effects of the complex I inhibitor rotenone on membrane dynamics occurring between mitochondria and peroxisomes. Using fluorescence microscopy, including quantitative assessment of ROS production with H_2DCFDA, and immunoblotting they found that rotenone treatment had substantial effects on both peroxisomes and mitochondria in COS-7 cells. With respect to peroxisomes, rotenone affected both morphology and intracellular distribution through a mechanism independent of mitochondrial generated oxidative stress, but dependent upon microtubule destabilization. Interestingly, in contrast, the opposite situation occurred with the effect of rotenone on mitochondrial morphology: these effects were dependent upon the generation of ROS, but independent of microtubule stabilization.

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These studies by Passmore et al. (2017) indicate that the intracellular mechanisms responsible for the redox communication between mitochondria and peroxisomes are likely complex, involving more than diffusion of ROS between organelles. Moreover, the authors also provide a cautionary note for investigations using rotenone to study Parkinson's disease: though it is widely held that mitochondrial dysfunction plays a key role in this disease process, the microtubule-destabilizing effects of rotenone on intracellular peroxisomal dynamics need also be considered.

Retinoic acid regulates growth plate cartilage septoclast biology and function

Septoclasts are located at the junction between the growth plate cartilage and the metaphysis and are involved in the resorption of the uncalcified cartilage matrix (Schenk et al. 1967). Previously, Bando et al. (2014) demonstrated the presence of epidermal-type fatty acid binding protein (E-FABP, FABP5) in septoclasts of mice. Retinoic acid is known to be bound by E-FABP and is normally present in the growth plate cartilage. Now Bando et al. (2017) show that under experimental conditions of excess amounts of retinoic acid or of vitamin A deficiency, the number of E-FABP- and peroxisome-proliferator-activated receptor-positive septoclasts is significantly decreased which is due to increased apoptosis. Under conditions of excess amounts of retinoic acid, septoclasts also had shorter and fewer cellular processes, which are cell surface specializations important for the resorption of the transverse septa of the growth plate cartilage. These experimental results indicate that endogenous levels of retinoic acid may be involved in the regulation of septoclast resorptive function.

Hepatocyte-specific depletion of ubiquitin regulatory X domain-containing protein 8 results in enhanced fibrosis in non-alcoholic steatohepatitis

Non-alcoholic fatty liver disease is a most common chronic liver disease in man (Williams et al. (2011), which may progress into non-alcoholic steatohepatitis (NASH), liver cirrhosis, and hepatocellular carcinoma. To further study the pathogenesis of NASH, Imai et al. (2017) examined the role of the ubiquitin regulatory X domain-containing protein 8 (UBXD8), which is critically involved in apolipoprotein B100 degradation, by investigating hepatocyte-specific UBXD8-deficient mice (U8-HKO) (Imai et al. 2015). When fed a very high fat diet or a choline-deficient very high fat diet for only 2 weeks, U8-HKO mice developed steatosis combined with perisinusoidal and periportal fibrosis. The extent of hepatic fibrosis could be reduced to that of control mice by the simultaneous administration of an angiotensin 2 type 1 receptor indicating the involvement of inflammation in the process. Together, the results demonstrate the importance of UBXD8 in liver physiology, and that lack of its function leads to liver fibrosis under conditions of dietary stress.

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