RESEARCH HIGHLIGHTS

Imaging microtubule dynamics

Metaphase spindles are highly dynamic structures, and have a higher concentration of microtubules than the surrounding cytoplasm. Spindle microtubules have been proposed to be stabilized by the local environment, for example through proximity to chromatin. Single-molecule imaging studies now suggest that spindle stabilization does not play a part in spindle assembly in *Xenopus laevis* egg extracts (*Mol. Biol. Cell* **21,** 323–333; 2010).

Mitchison and colleagues monitored the turnover of individual tubulin molecules at non-kinetochore microtubule ends. The growing and shrinking of microtubles could be explained by a simple mathematical model, allowing for quantitative analysis of the data. The kinetics of microtubule turnover was uniform across the spindle and did not change after inhibition of the motor kinesin-5. Moreover, dynamics of non-spindle microtubule arrays nucleated by Tetrahymena basal bodies was very similar to that of spindle microtubules. Thus, the authors conclude that non-kinetochore microtubules are not stabilized by the spindle environment, and have ruled out a major role for kinesin-5 and microtubule sliding in regulating microtubule turnover.

In this system, therefore, spindle assembly can occur without microtubule stabilization. The authors propose that the local high concentration of microtubules in the spindle is caused by spatially controlled nucleation, the regulation of which remains to be understood. CKR

IAPs play double in metastasis

The dissemination of tumour cells to distant organs during metastasis requires an increase in cell survival. This has been shown to depend partly on deregulated expression of members of the inhibitors of apoptosis protein (IAP) family, which normally keep caspases in check to inhibit apoptosis. Altieri and colleagues (*Cancer Cell*, **17,** 53–64; 2010) now report that the IAPs Survivin and XIAP also promote metastasis in a caspase-independent manner.

The authors observed that *XIAP* or *Survivin* knockdown impairs invasion of breast, prostate and colon metastatic cancer cell lines *in vitro*. Conversely, expression of Survivin in MCF-7 non-invasive breast cancer cells converts them into migratory cells that readily metastasize to the liver in an XIAP-dependent manner when injected into mouse spleen. Mutational analysis showed that the metastatic function of IAPs is independent of their pro-survival properties. Further experiments demonstrated that XIAP and Survivin act by promoting NfκB activation, which in turn upregulates fibronectin; human tumours showed correlative expression of IAPs and fibronectin. The IAP complex also induces β1-integrin signalling and activates FAK and Src kinases, all known positive regulators of motility, and depends on their activity for its metastatic effects.

These studies highlight the therapeutic potential of targeting IAPs, not only to induce apoptosis, but also to prevent invasion. NLB

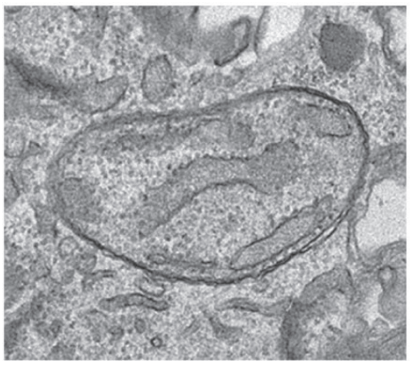
Jnk1 loss in the brain restricts obesity

The kinase Jnk1 is a central regulator of obesity associated with a high-fat diet. However, the organ in which Jnk1 functions to regulate this process had not been identified. Davis and colleagues now show that Jnk1 loss in the central nervous system prevents diet-associated obesity by affecting pituitary function (*Genes Dev. 24, 256-264; 2010*).

Mice with a targeted deletion of Jnk1 in the central nervous system did not gain weight when maintained on a high-fat diet. These mice also had a higher body temperature than their wild-type littermates, suggesting that Jnk1 might regulate pituitary hormones that control homeostasis. Indeed, thyroid hormone levels were higher in Jnk1-deficient mice than in wild-type mice, whereas adrenocorticotropic hormone and growth hormone expression was reduced. Intriguingly, thyrotropin-releasing hormone and thyroid-stimulating hormone mRNA levels, which are negatively regulated by thyroid hormone, were increased, indicating that Jnk1 deficiency in the brain upsets an aspect of this negative-feedback mechanism.

Pharmacological inhibition of thyroid hormone production in Jnk1-deficient mice reversed the phenotype, confirming the importance of thyroid hormone in Jnk1-mediated resistance to diet-induced obesity. The mechanism by which Jnk1 regulates thyroid hormone levels, and whether this pathway can be exploited therapeutically, awaits further investigation. EJC

Moving autophagosomes



A report published in the *Journal of Cell Biology* identifies a protein called FYCO1, which mediates microtubule plus-end directed movement of autophagosomes (*J. Cell Biol.* **188,** 253–269; 2010).

During autophagy, cytosolic cargo is sequestered in double-membraned compartments called autophagosomes that ultimately fuse with the lysosome, resulting in degradation of the autophagosomal contents. Johansen and colleagues have identified FYCO1 as a protein that interacts with LC3, which acts early in autophagosomal biogenesis, and show that it localizes to the outer membrane of autophagosomes. FYCO1 also interacts preferentially with GTP-bound Rab7, the GTPase implicated in autophagosome–lysosomal fusion, and Rab7 recruits FYCO1 to autophagosomes. FYCO1 overexpression redistributes autophagosomal structures to the cell periphery, whereas its depletion results in their clustering in the perinuclear region, suggesting a role for FYCO1 in autophagosome transport.

The authors propose a model wherein signals inducing autophagy may trigger binding of FYCO1 to microtubule plus-end directed motors and redistribution of pre-autophagosomal membrane during autophagy. Determining whether and how FYCO1 is regulated by upstream signalling and identifying the motors involved is a task for future research. SS

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