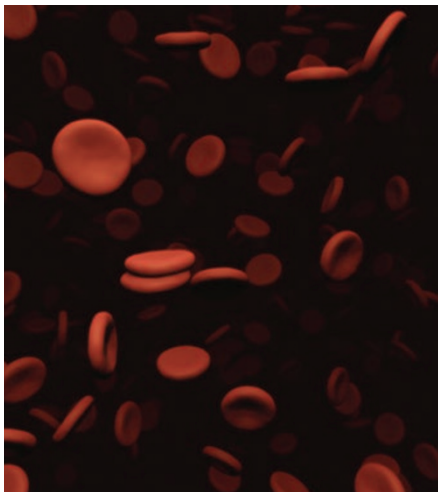
Neural blood ties



The vasculature contributes to stem cell niches in a number of tissues. However, despite evidence of a close relationship between neural stem cells (NSCs or astrocytes) of the subventricular zone (SVZ) and blood vessels, a role of the vasculature in the SVZ niche had not been documented. Two studies, from Doetsch and colleagues (*Cell Stem Cell* **3,** 279–288; 2008) and Temple and colleagues (*Cell Stem Cell* **3,** 289–300; 2008), now provide *in vivo* evidence for a rich plexus of blood vessels in the SVZ stem cell niche with specialized properties functionally relevant to the niche. Using quantitative confocal imaging of whole-mount preparations that preserves the three-dimensional relationship between cells, these studies demonstrate how NSCs and their transit-amplifying progeny are spatially organized and directly apposed to vessels at specific sites of adhesion. These specialized neurovascular interfaces, unique to the SVZ, are devoid of astrocyte endfeet and pericyte coverage — constituents of the blood-brain barrier – and thus more permeable to blood-borne substances. Chemical ablation of the stem cell progeny and labelling with proliferation markers showed that SVZ regeneration and neurogenesis are closely associated with these sites. Inactivation of the lamin receptor α6β1 integrin impaired adhesion of NSCs to endothelial cells and vessels, affecting the spatial distribution and proliferation of NSCs *in vivo*. Thus, α6β1 integrin is essential for anchoring SVZ stem cells to the vascular niche and for their function. SG

A non-coding RNA cascade for robust expression

Transcriptome analysis and high-throughput sequencing have shown that cells swarm with non-coding transcripts. Ohta and colleagues (*Nature* **455,** doi:10/1038/nature07348; 2008) report that non-coding RNAs initiated upstream of the *fpb1*$^+$ coding region, which is involved in gluconeogenesis, induce chromatin remodelling events required for *fbp1*$^+$ expression in response to glucose starvation in *Schizosaccharomyces pombe*. The sequential appearance of these long and rare non-coding RNAs during glucose starvation coincided with the stepwise 5′- to 3′-shift of RNA polymerase II binding to the promoter driving *fbp1*$^+$ transcription and the opening of chromatin. A transcription terminator upstream of the canonical start site prevented these events and thus *fbp1*$^+$ activation, indicating that expression of the non-coding transcripts is required for transition to a transcriptionally active state. The authors also show that sequential expression of the non-coding RNAs leads to recruitment of the transcriptional activators Atf1 and Rst2 to the upstream region of the coding sequence, and to stabilization of RNA polymerase II at the transcriptional start site. High-density tiling array analysis revealed the existence of related non-coding RNAs in the transcriptome, many containing an Rst2 binding site. Thus, initiating efficient gene transcription with non-coding RNAs may be a widespread phenomenon. NLB

mTOR inhibitors axe axons

Tuberous sclerosis complex (TSC) is produced by mutations in the Tsc1/Tsc2 complex, which negatively regulates mTOR. As mTOR signalling regulates cell size and growth, TSC is associated with disorganized overgrowth in several organs. However, TSC patients also have neurological problems, such as epilepsy and mental retardation. He and colleagues (*Genes Dev.* **22,** 2485–2495) now show an unexpected role for Tsc1 and Tsc2 in axon formation that may underlie the neurological symptoms. The mTOR pathway was activated and TSC2 inactivated in the axons of cultured hippocampal neurons and in mouse brain slices. Notably, localization of inactivated TSC2 in early stages of neuronal polarization suggests a role in the selection of a single neurite to become the axon. Overexpression of Tsc1 and Tsc2 resulted in 'axonless' neurons, and loss of Tsc1 or Tsc2 resulted in neurons with multiple axons. In mouse embryos, Tsc1 depletion caused ectopic axon formation, confirming its role in restricting axonal outgrowth. In most cell types mTOR controls translation, but the authors could not observe general changes in protein levels between wild-type and Tsc1-deficient hippocampal neurons. Instead, Tsc1/Tsc2 seems to selectively control the levels of neuronal polarity proteins SAD-A and SAD-B. However, knockdown of *SAD-A/B* only partially rescued the multiaxonal phenotype, suggesting that other targets of the Tsc/mTOR pathway also control neuronal polarity. CKR

Adhering before splitting

Pellinen *et al.* suggest that integrin-mediated cell adhesion is important for cytokinesis (*Dev Cell.* **15,** 371–385; 2008). Rab21-mediated integrin trafficking to the cleavage furrow seems to be crucial for the successful completion of cell division. The authors show that β1-integrin localizes to the cleavage furrow and that anti-integrin antibodies cause cytokinetic arrest. Live-cell imaging revealed that Rab21, a GTPase previously implicated in β1-integrin endocytosis, colocalizes with β1-integrin in vesicles at the ingressing cleavage furrow. Later, these vesicles localize to the poles of daughter cells. Perturbing integrin trafficking by depleting Rab21 or by using integrin mutants that cannot bind Rab21, results in aberrant cytokinesis, as assessed by the presence of multinucleate cells. β1-integrin mutants that are incapable of endocytosis are also unable to support productive cytokinesis. Finally, the authors demonstrate that Rab21 is deleted in an ovarian cancer cell line in which there is an increase in the number of multinucleated cells; this defect can be rescued by expressing wild-type Rab21. A failure in integrin trafficking and cytokinesis may lead to genetic instability and promote tumour progression. SS

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