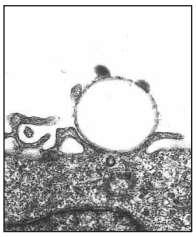
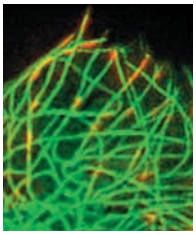


## InlB: a bacterial tyrosine kinase receptor agonist

Synthesis of proteins that mimic natural host cell ligands and induce uptake of bacteria expressing them is an effective invasion strategy used by several pathogenic bacteria. *Listeria monocytogenes*, which causes serious infections in immunocompromised individuals and pregnant women, produces two such proteins: InlA and InlB. In a Commentary on p. 3357, Hélène Bierne and Pascale Cossart discuss work that is shedding light on how InlB functions. The protein binds to hepatocyte growth factor receptors (HGF-Rs) on the surface of hepatocytes, epithelial cells and endothelial cells. This stimulates internalization of the bacterium by a mechanism similar to phagocytosis: the cell extends membrane around the particle and forms a continuous F-actin cup, which is disassembled following engulfment. Interestingly, in addition to stimulating pathways required for phagocytosis, InlB has other effects on target cells. It acts as a tyrosine kinase receptor agonist, regulating signalling cascades involving phospholipase Cγ1, Akt and NF-κB. This could be important after internalization and might promote cell survival once the bacterium is released into the cytosol.

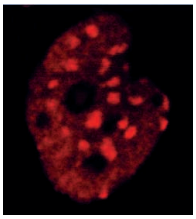
## Central vs peripheral circadian oscillators

Circadian oscillators are time-keeping mechanisms that cells use to maintain a 24 hour rhythm and drive periodic expression of genes controlling physiology, metabolism and behaviour. In each oscillator, two interlocked transcriptional and translational feedback loops ensure that the mRNA levels of transcription factors such as Clock (CLK) oscillate out of phase with those of proteins such as Period (PER) that oppose their effects. In a Commentary on p. 3369, Nicholas Glossop and Paul Hardin compare the central 'master' clock in the brain with peripheral clocks present in other tissues. Recent work indicates that the central oscillators differ significantly from their peripheral counterparts – for example, in the fly, peripheral oscillators require the blue-light-responsive protein cryptochrome (CRY) whereas the central oscillator does not. Furthermore, studies such as analyses of clock component mRNA cycling have revealed that peripheral oscillators from different species are strikingly similar. On the basis of these observations, Glossop and Hardin argue that the peripheral oscillators from different species reflect a basic clock design, from which central oscillators subsequently diverged.



## Microtubule dynamics in the cell interior

Numerous studies have shown that in vivo a key feature of microtubules is their dynamic instability – rapid switching between phases of elongation and shortening. For technical reasons, these studies have all examined microtubules at the cell periphery. Do microtubules in the cell interior behave the same way? Yulia Komarov and co-workers have addressed this question, using several novel experimental approaches (see p. 3527). These include analysis of the growth of fluorescently tagged microtubules through laser-photobleached centrosomes, direct observation of microtubules in centrosome-containing cytoplasts, tracking of GFP-tagged microtubule-binding proteins, and sequential subtraction analysis of regional differences in microtubule behaviour. The major finding is that, whereas at the periphery microtubule plus ends show dynamic instability, in the cell interior shortening events are infrequent and so the plus ends continue to grow. The authors propose that newly nucleated microtubules grow out rapidly from centrosomes towards the cell periphery and, once there, experience a 'boundary effect' that induces catastrophe (the switch from elongation to shortening) followed by cycles of elongation and shortening characteristic of peripheral microtubules.

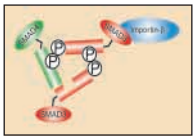


## Regulated targeting of TIF1β to heterochromatin

TIF1β is a developmentally regulated transcriptional co-repressor proposed to function by reorganizing higher-order chromatin structure. It is essential for early embryogenesis and interacts with heterochromatin-associated protein 1 (HP1), a heterochromatin component implicated in *Drosophila* position effect variegation – the heritable pattern of silencing produced by positioning of genes close to pericentric heterochromatin. Speculating that nuclear compartmentalization of TIF1β might be important for its function, Pierre Chambon and co-workers have examined its subnuclear distribution during differentiation of F9 embryonal carcinoma cells (see p. 3439). They find that TIF1β has a dispersed (euchromatic) distribution in the nucleoplasm of undifferentiated cells but relocates to centromeric heterochromatin following differentiation induced by retinoic acid. No such relocation occurs in growth-arrested cells or RA-resistant cells. The authors show that mutation of the TIF1β PxVxL motif that mediates interactions with HP1 blocks targeting of TIF1β to centromeric heterochromatin. They therefore conclude that nuclear compartmentalization of TIF1β is dynamically regulated by HP1 interaction during differentiation, speculating that TIF1β might mediate cell-type-specific gene silencing by recruiting target genes to the transcriptionally inactive heterochromatic compartment.

## Metalloproteinase-dependent tubulogenesis

The formation of new blood vessels is critical for development, wound healing and tumour progression. A variety of angiogenic factors, including vascular endothelial growth factor (VEGF) and fibroblast growth factor 2 (FGF-2), regulate the process, and matrix metalloproteinases (MMPs) are thought to participate in the matrix remodelling required. Dylan Edwards and co-workers have examined the interplay between these proteins during remodelling of endothelial cells in 3D fibrin matrices – a useful model system that, unlike 2D cultures, mimics the microenvironment at sites of vascular injury (see p. 3427). The authors observe that endothelial cells undergo tubulogenesis when cultured in these matrices, showing that tubulogenesis is enhanced by VEGF, FGF-2 and hepatocyte growth factor (HGF/SCF) and accompanied by upregulation of several *MMP* genes. They also find that the MMP inhibitors TIMP-2 and TIMP-4, which target membrane-type MMPs (MT-MMPs), block VEGF/FGF-2-stimulated tubulogenesis but that inhibitors of soluble MMPs (e.g. MMP-2) do not. Edwards and co-workers conclude that MT-MMPs represent a subgroup of MMPs crucial for angiogenesis and therefore constitute enzymes that could be selectively targeted by antiangiogenic therapies.



## The Smad network

Signalling by members of the transforming growth factor β (TGF-β) superfamily depends on a group of intracellular signalling molecules termed Smads. R-Smads are phosphorylated by the Ser/Thr kinase receptors to which these ligands bind; the R-Smads can then heterodimerize with a Co-Smad, enter the nucleus and regulate gene expression. In Cell Science at a Glance (see p. 3355 + poster), Aristidis Moustakas surveys the Smad signalling network, detailing its cytoplasmic and nuclear aspects, as well as the regulatory mechanisms that operate.

## In the next issue of JCS

**Sticky Wicket**

**What is it about white hair and the rumpled, crumpled look that makes you a scientist?** Caveman

**Cell Science at a Glance**

**Calponin homology domains at a glance.** E. Korenbaum and F. Rivero

**Commentaries**

**The spindle assembly checkpoint.** J. Zhou et al.

**Calcium wave pacemakers in eggs.** R. Dumollard et al.

**Research Articles**

**A chk1-dependent G1 checkpoint.** M. Synnes et al.

**Delivery of MDP modulate rab expression.** K. Mukherjee et al.

**SNARE involvement in AQP2 translocation.** S. Gouraud et al.

**Binding of Sly1 to Sed5 enhances SNARE complex formation.** Y. Kosodo et al.

**FGF-2 translocation to the extracellular surface.** A. Engling et al.

**Regulation of phagosome fusion.** E. Harris and J. Cardelli

**CAR formation checkpoint in *S. pombe*.** D. P. Mulvihill and J. S. Hyams

**Oligodendrocyte development from ES cells.** N. Billon et al.

**Wound-induced binding of USF-1 to the PAI-1 E Box.** K. M. Providence et al.

**Role of Rap1 in cell viability and osmotic stress.** R. Kang et al.

**Localization of Asy1 on meiotic chromosomes.** S. J. Armstrong et al.

**Has2 control of keratinocyte migration.** K. Rilla et al.

**Roles of C/EBPβ/δ in IRS-2 and GLUT4 expression.** H. Yamamoto et al.

**Role of aPKC in epithelial junction formation.** A. Suzuki et al.

**PKCα-mediated MAPK activation during myogenesis.** A. Mauro et al.