**In Brief**

**Homing in on CD44**

Dimitroff et al. (page 1277) appear to have uncovered the major “homing receptor” that allows hematopoietic progenitor cells (HPCs) to enter bone marrow. The discovery of the receptor, a novel glycoform of CD44, could form the basis for improvements in HPC selection for hematopoietic stem cell transplants.

The endothelial proteins that are believed to mediate homing include E-selectin. This membrane protein functions in the “rolling” phase of leukocyte–endothelial adhesive interactions, and its expression on vascular endothelium is typically induced by inflammatory stimuli. But its expression on bone marrow sinusoidal endothelium, where it is believed to mediate HPC homing to marrow, is constitutive. Until now, the corresponding ligands on HPCs have remained poorly characterized.

In the new work, the authors used a novel blot rolling adherence assay to survey all possible E-selectin ligands expressed on human HPCs. In addition to P-selectin glycoprotein ligand-1 (PSGL-1), which had previously been identified as an E-selectin ligand on HPCs, the screen identified a specific glycoform of CD44. This glycoform, which the authors call HCELL, mediates E-selectin–dependent rolling interactions over a wider shear range than PSGL-1. Intriguingly, whereas PSGL-1 is expressed on both mature and immature myeloid cells, HCELL expression is restricted to primitive human CD34+ bone marrow cells, suggesting that the newly discovered CD44 glycoform functions principally in directing human HPC homing to bone marrow.

**Building Worm Kinetochores**

Three papers in this issue present new data on kinetochore structure and assembly, and establish *Caenorhabditis elegans* as a relevant and accessible model system for future kinetochore studies. *C. elegans* differs from mammals in having holocentric centromeres, which are distributed along the chromosome, but the new work illustrates that the machinery of kinetochore assembly is highly conserved.

Moore et al. (page 1199) identify a *C. elegans* homologue of the mammalian kinetochore structural component CENP-C; the same group had previously found worm homologues of CENP-F and the histone H3 variant CENP-A. In the new work, the authors discover that *C. elegans* CENP-C is cytoplasmic in interphase, but localizes to the nucleus (specifically the centromere) in mitosis. This centromeric localization requires the worm CENP-A homologue, and both CENP-A and CENP-C are required for the localization of CENP-F, pointing to an ordered assembly pathway for kinetochore components. Inhibiting the expression of worm CENP-C causes a failure both in forming two separate sister centromeres on sister chromatids and in creating a functional kinetochore.

By electron microscopy with high-pressure freezing followed by freeze substitution, Howe et al. (page 1227) demonstrate that the kinetochore in mitotic and meiotic *C. elegans* cells is similar to the mammalian kinetochore. The authors also show that HIM-10, a highly conserved protein related to the Nuf2 kinetochore proteins, is required for worm kinetochore structure and function, and depleting HIM-10 appears to cause a defect in spindle attachment to chromosomes.

**Getting to Know TOM**

The TOM complex is a protein-conducting channel located on the outer membrane of mitochondria that facilitates the transfer of preproteins through the membrane. After purifying the Tom40 protein from *Neurospera crassa*, Ahting et al. (page 1151) performed a detailed biophysical characterization of the protein, uncovering new information on the structure of the TOM complex. The results partially contradict earlier studies that ex-
The previous work had shown that Tom40 is the key structural component of the channel in *Neurospora crassa* and *Saccharomyces cerevisiae*, and can indeed form a channel by itself. Ahting et al. demonstrate that their preparation of Tom40, purified from *Neurospora* TOM core complexes, can also assemble into pores. But, in comparison with the bacterially derived Tom40 pores, the new pores had gating properties and conductance levels closer to those of TOM core complexes.

The structure of the purified and bacterially derived pores also seems to differ. Spectral analysis of the purified Tom40 reveals a secondary structure containing no more than 31% β-sheet topology, significantly less than the 48% β-sheet content of mitochondrial porins. This contrasts with earlier results from bacterially expressed *S. cerevisiae* Tom40, which was proposed to be structurally similar to members of the porin family. Ahting and colleagues suggest that the gentle purification of Tom40 from the functional complex conserved the in vivo higher-order structure of the protein.

**Focal Complexes: Pull Them and They Grow**

Using a micropipette to tug on a cell’s surface, Riveline et al. (page 1175) were able to examine the effects of external forces on the development of focal contacts. The results demonstrate that the activation of focal complex growth is a local phenomenon in which focal contacts operate as mechanosensors. In addition, the authors gained substantial new insight into the regulation of focal contact growth by downstream targets of the G-protein Rho.

Previous work suggested that focal complexes required local mechanical tension in order to develop into larger focal contacts, but this hypothesis had not been tested directly. In the new work, external pulling with a micropipette mimicked forces normally generated by cell contractility in areas where focal complexes are formed. When force is applied to a focal complex, the complex recruits new proteins, elongates, and becomes indistinguishable from a normal focal contact. Among Rho downstream targets, mDia1 is still required for focal contact assembly even after force is applied, but Rho kinase (ROCK) is now dispensable.

The results suggest that cells normally use a ROCK-dependent mechanism to create contractile force, which, in combination with an mDia1-dependent input, causes focal complexes to grow. In this model, focal contacts act as mechanosensors to determine the local balance between cell-generated force and extracellular matrix rigidity.