A building block of two organelles

O
n page 185, Kondylis and Rabouille find that a protein required for Golgi structure also organizes transitional ER (tER) sites, also known as ER exit sites. Although addressing tER assembly, the results might also influence models of Golgi formation. tER sites are enriched in COPII vesicles containing proteins destined for the Golgi. In fly S2 cells, tER sites are found adjacent to well-defined Golgi stacks. The authors have found that tER organization in S2 cells depends on dp115, of which mammalian homologues are necessary for vesicle transport and Golgi structure. In the absence of dp115, small tER sites that were no longer spatially associated with the Golgi were scattered throughout the cytoplasm.

As expected, Golgi stacks were fragmented into vesicles and tubules in dp115-depleted cells. Transport was not inhibited, however, so at least in S2 cells, Golgi structure and function are not necessarily linked. Golgi fragmentation did not cause the tER disorganization, as depletion of syntaxin 5 disrupted Golgi stacks but not tERs. Rather, dp115 probably has a separate function as a component of a recently proposed matrix surrounding tERs. The authors found that dp115 is as abundant in the tER as it is in the Golgi complex. The protein may help build the tER through its interaction with the COPII coat.

Neural cells turn and run

W
hen your gut tells you to run, it is wise to listen. Embryonic neural precursors do just that, according to De Bellard et al. (page 269), who identify the basis of an avoidance mechanism for migrating neural crest cells.

Groups of embryonic neural precursors take separate paths on their way to forming the peripheral nervous system. Vagal cells, which emerge from the neck region, migrate long distances to enter the gut. Cells in the trunk originate closer to the gut yet never enter this region. The new results show that the gut is off limits because trunk cells sense Slit proteins, chemorepellents involved in axon guidance in flies and vertebrates.

In chick embryos, Slit expression marked the entrance to the gut. The group injected Slit-expressing cells into embryos and found that trunk cells stopped in their tracks to avoid migrating through regions containing the chemorepellent. Vagal cells, in contrast, were unaffected by Slit proteins, as trunk but not vagal cells express the Slit receptors Robo1 and Robo2.

Repulsion required contact between trunk cells and cells expressing surface-bound Slit. Slit administered in vitro is reused uniformly, so a simple repulsion effect is not obvious. But this form of Slit does cause trunk cells to migrate faster than vagal cells. In vivo, these two effects may combine to turn trunk cells away from the gut and speed their migration in the other direction.

Kicking out antiviral proteins

L
ike a bouncer at a club, the Epstein Barr virus (EBV) LMP1 protein removes a threatening presence by ejecting cellular proteins from the nucleus, according to Ohtani et al. on page 173.

EBV infection leads to excessive cell proliferation that can cause disorders such as carcinoma and lymphoma. Cells normally prevent unusual proliferation by inducing the p16\(^{INKA}\)/RB-dependent senescence pathway. But the authors show that EBV bypasses this failsafe by relocating transcription factors for this pathway to the cytoplasm.

Nuclear export was induced by the viral protein LMP1. EBV infection or LMP1 expression caused the export of Ets2, the inducer of p16\(^{INKA}\) transcription. LMP1 also kicked out transcription factors E2F4 and E2F5, which normally act downstream of p16\(^{INKA}\) to prevent cell cycle progression. LMP1 induces export of its targets by increasing their affinity for CRM1, which directs the major nuclear export pathway in mammalian cells. The molecular details are unclear as yet, but the authors find that the MEK pathway is required for E2F4 export. Perhaps phosphorylation of E2F4 makes it more attractive to CRM1.

Immortalization of human cells requires inactivation of both RB and p53 pathways, so LMP1 or another EBV protein may also cause the export of p53-related proteins. Ohtani et al. found that at least some other cell cycle proteins containing nuclear export signals are resistant to LMP1. If LMP1 targets only a few proteins for export, it might be possible to develop drugs to limit EBV infection with few side effects.