Position of power

Migrating leukocytes are “rear-wheel drive cells,” says Antonella Viola. Her group finds that mitochondria, the cell’s engines, shift to the back of neutrophils to power cell movement, as revealed in Campello et al. (page 2879).

Mitochondria can accumulate in regions of the cell with high energy demands, such as at the active growth cones of developing neurons and at the neuromuscular synapse. Viola and her team wondered whether mitochondria might also adopt a specific intracellular location in migrating cells. Leukocytes migrate to immunological battlegrounds in response to chemokines, and the team now shows that, in vitro, this chemotaxis is coupled with movement of mitochondria to the rear of the cell, known as the uropod.

Although the leading edge of the leukocyte sends out exploratory protrusions as these cells migrate, the uropod contains both the adhesion machinery and the myosin motors essential for cell movement, explains Viola. The discovery that mitochondria also relocate to the uropod leads Viola to suggest that, in the mechanics of cell migration, the power comes from the push.

Mitochondrial movement along microtubules requires the mitochondria to first divide into smaller, mobile units. By preventing this division, the team revealed that mitochondrial relocation to the uropod was not just coupled with, but necessary for, leukocyte migration.

Boosting the mitochondrial energy production in these cells compensated for a lack of relocation, suggesting that mitochondrial movement was required for localizing ATP production at the uropod. Indeed, the team showed that inhibiting mitochondrial, but not cytoplasmic ATP production, reduced activation of myosin motors in the uropod but not elsewhere in the cell.

In addition to various leukocytic cell types, migrating human breast cancer cells also relocate their mitochondria to the rear, the team found. This suggests that inhibiting the division of mitochondria, and thus their movement, might be a potential intervention strategy for preventing tumor metastasis. JEM

Hunting for histamine’s source

For asthma sufferers, contracting a lung infection can mean hospitalization, but it has never been clear how bugs exacerbate allergic conditions. Xu et al. (page 2907) now show that the major allergic inflammatory mediator—histamine—is also produced in response to infection. But it comes from an unexpected source.

Mast cells together with basophils are considered the major producers of histamine. Because bacterial infection of the lung can lead to asthma attacks more severe than those caused by allergens, Caughey’s group hypothesized that histamine might be produced in response to infection. But it comes from an unexpected source.

The team found that, approximately one week after infection with *Mycoplasma pulmonis* bacteria, histamine levels in the lungs of the mice had risen dramatically. However, this increase was observed even if the mice had no mast cells. The team noticed that the rising level of histamine paralleled an increase in the number of neutrophils in the lung. Considering the possibility that these cells might be the source of the histamine, the team depleted neutrophils in the mast cell-deficient mice and, sure enough, observed a concurrent drop in the level of infection-induced histamine.

Although neutrophils have previously been reported to produce histamine, their contribution was thought to be small. The vast amount of histamine they produce in response to lung infection—an approximately 50-fold induction—was therefore a surprise, says research leader, Caughey.

The team now plans to see whether other bacteria induce a similar increase in the production of histamine, and whether high histamine levels are also a feature of human lung infections. If so, Caughey suggests that antihistamines, not generally considered in the treatment of infection, deserve a second look. JEM