The mystery of the (not) missing coenzyme

Lapointe et al. reveal that the partial depletion of a mitochondrial enzyme inhibits respiration by altering the distribution of the coenzyme ubiquinone (UQ). The mitochondrial hydroxylase MCLK1 helps to synthesize UQ (also known as coenzyme Q), which transfers electrons along the respiratory chain of the mitochondrial inner membrane and also serves as an antioxidant there and in other cellular membranes. Though Mclk1-null mice die during embryogenesis, mice with a single copy of the Mclk1 gene live longer than wild-type animals, possibly because their metabolism is altered by a reduction in mitochondrial respiration. Yet UQ levels appear to be unchanged in Mclk1 heterozygotes, leaving it unclear why these animals have dysfunctional mitochondria.

Sec and Tat share the workload

Keller et al. describe how two transport pathways cooperate to insert a bacterial protein into the cell membrane. Bacteria and chloroplasts have two different systems that translocate proteins across or into membranes. The Sec pathway transports unfolded proteins through the SecYEG membrane channel, whereas the twin-arginine transport (Tat) machinery translocates proteins such as the Rieske redox protein, whose C-terminal iron-sulphur domain must be carefully folded in the cytosol before being transported across the membrane. The Rieske proteins of Streptomyces coelicolor and other actinobacteria, however, contain more transmembrane domains (TMDs) instead of one and have N termini that lack the twin-arginine motif usually recognized by the Tat machinery. How these bacteria insert their Rieske proteins into membranes is therefore unclear.

Tiam1 increases turnover

The guanine nucleotide exchange factor Tiam1 promotes cell migration by regulating the turnover of cell-matrix adhesions, Wang et al. reveal. Migrating cells polarize to form a protrusive front and a retracting tail. The Rac GTase helps establish and maintain this polarity by stimulating membrane protrusion and promoting the rapid turnover of integrin-based adhesions at the cell’s leading edge. Integrins activate Rac in response to cell adhesion, but how they do this is unclear. Wang et al. found that Tiam1, a Rac activator required for polarized cell migration, binds to talin, an adaptor protein that connects integrins to signaling molecules and the actin cytoskeleton.

Tiam1 colocalized with talin at adhesions, particularly at the cell front, but was displaced when talin was depleted by RNAi. Cells lacking either talin or Tiam1 showed decreased Rac activation in response to integrin adhesion, delaying cell spreading and polarization. And adhesion turnover was slower at the leading edge, thus inhibiting cell migration. Talin-deficient cells could be rescued by the re-expression of wild-type talin but not of talin mutants unable to bind or recruit Tiam1 to adhesions.

Tiam1’s localization to adhesions was also regulated by the PAR polarity complex, which binds to Tiam1 through PAR3 and phosphorylates it via atypical protein kinase C (aPKC). Depleting PAR3 or inhibiting aPKC prevented adhesion-induced Rac activation and cell spreading. The researchers speculate that the phosphorylation of Tiam1 by aPKC promotes the exchange factor’s association with talin, allowing integrin-based adhesions to stimulate Rac and promote polarized cell migration.