IN BRIEF

GENE EXPRESSION

Selective silencing of mutated mRNAs in DM1 by using modified hU7-snRNAs

François, V. *et al. Nature Struct. Mol. Biol.* **18**, 85–87 (2011)

Myotonic dystrophy type 1 (DM1) is an autosomal dominant genetic disease that is caused by expanded CTG repeats in the 3′ untranslated region of DM protein kinase (*DMPK*). Mutant RNAs containing multiple CUG repeats become trapped in the nucleus and cause misregulation of alternative splicing, which ultimately leads to neuromuscular dysfunction. Previous studies have used synthetic antisense oligonucleotides to target these mutant RNAs, but this has limited therapeutic potential given that the treatment needs to be given repeatedly. In this study, François *et al.* developed a modified version of the human U7 small nuclear RNA (U7-snRNA) that has part of its sequence replaced with a poly-CAG antisense sequence. Stable expression of this modified U7-snRNA in cells from patients with DM1 led to degradation of the mutant *DMPK* RNAs and restoration of normal splicing patterns of genes such as dystrophin.

AUTOPHAGY

Phosphorylation of ULK1 (hATG1) by AMP-activated protein kinase connects energy sensing to mitophagy

Egan, D. F. *et al. Science* 23 Dec 2010 (doi:10.1126/science.1196371)

UNC51-like kinase 1 (ULK1) and ULK2 are thought to initiate autophagy in mammalian cells under nutrient-limited conditions, but how they are activated was unknown. Egan *et al.* identify ULK1 and ULK2 as targets of AMP-activated protein kinase (AMPK) — an energy sensor that is activated when nutrients are low. AMPK interacts with ULK1 and ULK2, and it phosphorylates ULK1 on at least two sites. p62, which is known to be degraded during autophagy and recruited to mitochondria during mitophagy, was increased in AMPK- or ULK1-deficient hepatocytes, as was the number of abnormal mitochondria. Importantly, overexpressed ULK1 must be phosphorylated by AMPK to restore p62 degradation, autophagy and mitochondrial homeostasis in ULK1-null cells. Thus, AMPK that is activated in response to nutrient deprivation can activate ULK1 to promote mitophagy.

STEM CELLS

Dynamics between stem cells, niche, and progeny in the hair follicle

Hsu, Y.-C., Pasolli, H. A. & Fuchs, E. *Cell* **144**, 92–105 (2011)

During homeostasis, stem cells often exit their niche and become transit-amplifying cells, which proliferate and terminally differentiate; however, it was unclear when stem cells lose their self-renewal ability and commit to a lineage. Hsu *et al.* show that hair follicle stem cells lose their 'stemness' gradually while they proliferate downwards to form the outer root sheath (ORS). Early stem cell descendents, found in the upper ORS, are slow-cycling and retain their capacity to self-renew and make tissue. These cells survive the destruction phase of hair growth (catagen) and become the stem cell niche for the next hair cycle. By contrast, descendents that have progressed further along the ORS are fast-cycling. Surprisingly, they retain some stem cell markers, survive and can return to the niche, where they provide key inhibitory signals that instruct stem cells to stop making hair.