Nature Reviews Neuroscience | AOP, published online 11 June 2014;

IN BRIEF

NEURODEGENERATIVE DISEASE

Import blockade

Neuronal loss in Huntington's disease (HD) has been associated with mitochondrial dysfunction, but how mitochondrial defects are linked to the actions of mutant huntingtin (mHTT) — which causes HD — is unclear. Here, in brain slices from individuals with HD, mHTT aggregates colocalized with a subunit of the mitochondrial import inner membrane translocase 23 (TIM23) complex and dynamin-related protein 1 (proteins that reside in mitochondria), and pull-down experiments using mouse brain lysates showed that mHTT could bind to several TIM23 complex subunits. Mitochondrial protein import was inhibited in primary neurons expressing mHTT, and TIM23 complex overexpression ameliorated this impairment and prevented mHTT-induced neuronal death. This suggests that mHTT causes mitochondrial dysfunction by inhibiting protein import and that this is an early event in HD pathophysiology.

ORIGINAL RESEARCH PAPER Yano, H. *et al.* Inhibition of mitochondrial protein import by mutant huntingtin. *Nature Neurosci.* **17**, 822–831 (2014)

NEURAL NETWORKS

Getting rich young

Diffusion MRI and network analysis have revealed a series of cortical 'hubs' in the adult human brain that are highly connected to each other and thought to enable efficient communication between distal cortical regions. Ball *et al.* examined when such 'rich-club' architecture emerges by assessing connectivity in the developing human brain. At 30 weeks of gestation, cortical hubs were already highly connected, and from 30 to 40 weeks, there was a notable increase in connectivity between these hubs and other brain regions. Interestingly, preterm infants (at term-equivalent ages) showed alterations in this organization, including decreased connectivity between hub and subcortical regions. The cortical rich club is thus in place well before birth, and interactions between hubs and other brain areas develop late into gestation.

ORIGINAL RESEARCH PAPER Ball, G. *et al.* Rich-club organization of the newborn human brain. *Proc. Natl Acad. Sci. USA* **111**, 7456–7461 (2014)

BLOOD–BRAIN BARRIER

A dual-purpose facilitator

Two new studies reveal crucial roles for MFSD2A (major facilitator superfamily domain-containing protein 2A) in blood–brain barrier (BBB) development and function. Nguyen *et al.* showed in mice that MFSD2A was expressed in the endothelium that comprises the BBB at embryonic day 15.5 (E15.5) and in adulthood. *Mfsd2a*$^{-/-}$ mice exhibited various motor and cognitive deficits and decreases in neuronal number in certain brain regions. These mice also had low brain levels of docosahexaenoic acid (DHC), an omega 3 fatty acid, and cell-based assays revealed that MFSD2A can transport DHC when it is attached to the lipid lysophosphatidylcholine. In the other study, Ben-Zvi *et al.* established that the mouse BBB becomes functional at E15.5 and that this milestone is preceded by an increase in *Mfsd2a* expression in the CNS vasculature. They also found that embryonic and postnatal *Mfsd2a*$^{-/-}$ mice had a leaky BBB that was caused by increased CNS endothelial cell vesicular transcytosis. Thus, MFSD2A regulates both DHC transport into the brain and vesicle transport across the BBB.

ORIGINAL RESEARCH PAPER Nguyen, L. N. *et al.* Mfsd2a is a transporter for the essential omega-3 fatty acid docosahexaenoic acid. *Nature* **509**, 503–506 (2014) | Ben-Zvi, A. *et al.* Mfsd2a is critical for the formation and function of the blood–brain barrier. *Nature* **509**, 507–511 (2014)