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IN BRIEF

ALZHEIMER DISEASE

Increased risk of falls in preclinical Alzheimer disease

Patients with Alzheimer disease (AD) dementia are known to be at increased risk of falls, but whether this association exists in preclinical stages of AD was not known. In a 12-month longitudinal study of 125 cognitively normal individuals, Stark *et al.* have shown that those with biomarker evidence of preclinical AD are more likely to experience a fall than are people without presumptive AD. These results suggest motor changes could precede cognitive impairment during development of clinical AD.

Original article Stark, S. L. *et al.* Preclinical Alzheimer disease and risk of falls. *Neurology* doi:10.1212/WNL.0b013e31829d8599

AMYOTROPHIC LATERAL SCLEROSIS

Histone deacetylase 4—accelerator of progression in ALS?

During early stages of amyotrophic lateral sclerosis (ALS), motor neuron loss is compensated for by collateral innervation, which delays onset of muscle wasting. In a recent study of 11 patients with ALS, researchers identified increased muscle expression of histone deacetylase 4 (HDAC4) in patients with rapidly progressing disease compared with long-term ALS survivors. Moreover, HDAC4 expression levels were inversely correlated with extent of muscle reinnervation. Inhibitors of HDAC4 could, therefore, be a therapeutic option to slow disease progression in ALS.

Original article Bruneteau, G. *et al.* Muscle histone deacetylase 4 upregulation in amyotrophic lateral sclerosis: potential role in reinnervation ability and disease progression. *Brain* doi:10.1093/brain/awt164

CEREBROVASCULAR MALFORMATIONS

Endothelial-to-mesenchymal transition—role in cerebral cavernous malformation

Cerebral cavernous malformation (CCM) is caused by mutations in the genes *CCM1*, *CCM2* or *CCM3*, and is characterized by vascular lesions that can lead to cerebral haemorrhage. New research has shown that endothelium-specific ablation of *Ccm1* in mice leads to CCM pathology via endothelial-to-mesenchymal transition (EndMT) of transgenic cells via upregulation of TGF-β and bone morphogenetic protein signalling. Moreover, inhibition of these signalling pathways prevented EndMT and reduced vascular lesion load in the transgenic mice, pointing towards a therapeutic strategy for CCM.

Original article Maddaluno, L. *et al.* EndMT contributes to the onset and progression of cerebral cavernous malformations. *Nature* **498**, 492–496 (2013)

NEUROMETABOLIC DISEASE

Pioglitazone for treatment of X-linked adrenoleukodystrophy?

X-linked adrenoleukodystrophy is a neurometabolic disorder that results from inactivation of the peroxisomal ABCD1 transporter. A recent study in *Abcd1*-null mice found reduced mitochondrial DNA and downregulation of the mitochondrial biogenesis pathway. Importantly, activation of this pathway with the antidiabetic drug pioglitazone corrected the transgenic phenotype and prevented locomotor disability and axonal damage in these mice.

Original article Morató, L. *et al.* Pioglitazone halts axonal degeneration in a mouse model of X-linked adrenoleukodystrophy. *Brain* doi:10.1093/brain/awt143