Identification of a fifth adaptor complex and its link with hereditary spastic paraplegia

Hirst J, Barlow LD, Francisco GC, Borner GHH, Sahlender DA, Dacks JB, **Robinson MS**

CIMR, Addenbrooke's Hospital, Cambridge CB2 0XY, UK

Adaptor proteins form part of a vesicle coat machinery involved in sorting transmembrane proteins to different destinations in the cell. Using sequence homology searching it was thought that only four adaptor complexes existed. However, using structural homology searching we identified a fifth adaptor complex, and named it AP-5 (The fifth adaptor protein complex. **Hirst J** et al., 2011 PLoS Biol. Oct;9(10):e1001170). We were able to show that AP-5 is comprised of four subunits that associate in a complex on late endosomal membranes. In order to identify proteins that associated with AP-5 we performed native immunoprecipitations and found that in addition to the four subunits of AP-5 two other proteins were stably associated with AP-5, and these proteins were identified as SPG15 (FYVE-CENT/ ZFYVE26) and SPG11. Previously, SPG11 and SPG15 have been genetically linked through similar patient phenotypes, characterised by autosomal recessive hereditary spastic paraplegia with thin corpus callosum. Here, we provide evidence for the biochemical association of SPG11 and SPG15 as components of the AP-5 complex. Our working model is that SPG11 and SPG15 may act as components of the AP-5 'coat machinery' to provide a scaffold (as clathrin does for AP-1 and AP-2 adaptor complexes), and a means to regulate its membrane association.