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"Adaptor proteins (AP 1-5) are heterotetrameric complexes that facilitate specialized cargo sorting in vesicular mediated trafficking. Mutations in AP-5 have been reported to cause Hereditary Spastic Paraplegia (SPG48), though their impact at the cellular level has not been assessed. Here I present the characterization of three independent patient-derived fibroblasts harbouring nonsense mutations in AP5Z1. These patients present with neurological conditions, and from skin biopsies we have established patient-derived fibroblasts. In all three patient-derived lines we show that there is complete loss of AP-5 ζ protein and a reduction in the associated AP-5 μ5 protein. Using ultrastructural analysis we show that these patient-derived lines consistently exhibit abundant multilamellar structures that are positive for markers of endolysosomes, and are filled with aberrant storage material organised as exaggerated multilamellar whorls, striated belts and 'fingerprint bodies'. This phenotype can be replicated in a HeLa tissue culture model by siRNA knockdown of AP-5 ζ. The cellular phenotype bears striking resemblance to features described in a number of lysosomal storage disorders. Collectively, these findings reveal an emerging picture of the role of AP-5 in endosomal and lysosomal homeostasis, and illuminate a potential pathomechanism which is relevant to the role of AP-5 in neurons. Moreover, the resulting accumulation of storage material in endolysosomes leads us to propose that AP-5 deficiency represents a new type of lysosomal storage disorder."