## Microglial beclin 1 regulates retromer trafficking and phagocytosis and is impaired in Alzheimer's disease.

**Journal:** Neuron

**Publication Year:** 2013

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**PubMed link:** 24012002

**Funding Grants:** Systemic Protein Factors as Modulators of the Aging Neurogenic Niche

**Public Summary:**
Phagocytosis controls CNS homeostasis by facilitating the removal of unwanted cellular debris. Accordingly, impairments in different receptors or proteins involved in phagocytosis result in enhanced inflammation and neurodegeneration. While various studies have identified extrinsic factors that modulate phagocytosis in health and disease, key intracellular regulators are less understood. Here we show that the autophagy protein beclin 1 is required for efficient phagocytosis in vitro and in mouse brains. Furthermore, we show that beclin 1-mediated impairments in phagocytosis are associated with dysfunctional recruitment of retromer to phagosomal membranes, reduced retromer levels, and impaired recycling of phagocytic receptors CD36 and Trem2. Interestingly, microglia isolated from human Alzheimer's disease (AD) brains show significantly reduced beclin 1 and retromer protein levels. These findings position beclin 1 as a link between autophagy, retromer trafficking, and receptor-mediated phagocytosis and provide insight into mechanisms by which phagocytosis is regulated and how it may become impaired in AD.

**Scientific Abstract:**
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