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The involvement of progranulin for α -synuclein reduction through autolysosome formation

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Progranulin is a multipotent protein that contributes to various pathology such as inflammation and tumorigenesis. Absence of progranulin gene causes the onset of frontotemporal lobar degeneration (FTLD) and neural ceroid lipofuscinosis. Recently, it has been reported that some Parkinson's disease patients with α -synuclein lesions have a progranulin gene mutation. However, the relationship between progranulin and α -synuclein accumulation mechanism is unclear. We examined the effect of progranulin against α -synuclein accumulation.

We evaluated progranulin effects against MPP⁺ damage in human derived neuroblastoma cells (SHSY-5Y cells). A-synuclein and autophagy related factors (AMPK, mTOR, LC-3, p62) were evaluated by Western blot. To clarify autolysosome formation, we used DAL-Green, specific autolysosome detector.

A-synuclein expression was reduced by progranulin treatment. On the other hand, AMPK or mTOR activation were not changed. Furthermore, LC-3II/LC3-I ratio and p62 expression were reduced. These results indicate that progranulin ameliorated autolysosome formation decreased by MPP⁺.

These findings indicate that progranulin promotes autophagy degradation by inhibiting autolysosome formation and reduces α -synuclein accumulation.