# Applying autophagy as a treatment for Huntington's disease

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Huntington's disease, a fatal genetic disorder, leads to the breakdown of brain nerve cells due to mutated Htt protein aggregation, with no existing cure. This study proposes enhancing the degradation of both soluble and aggregated forms of mutant Htt (mHtt) through Chaperone-Mediated and Ubiquitin-Mediated Autophagy, employing Adeno-associated viruses (AAV) to deliver mRNA coding for autophagy-regulating proteins. Chaperone-mediated autophagy (CMA) selectively degrades proteins via the HSC70 chaperone and LAMP-2A lysosomal protein. For insoluble mHtt aggregates, Optineurin (OPTN), recognizing ubiquitinated proteins, is suggested. Enhancements include synthetic dimer QBP1 for HSC70 targeting mHtt, and AAV-delivered mRNA for producing HSC70, QBP1, and OPTN, aimed at crossing the blood-brain barrier (BBB). Early-stage Huntington's may benefit from CA77.1 to boost LAMP-2A, with later stages requiring AAV-mediated OPTN mRNA for degrading polyQ aggregates. The approach targets mHtt specifically, minimising wild-type HTT degradation. Repeated AAV treatments necessitate alternative vectors due to immune response risks. While focusing on mHtt degradation, gene editing is highlighted for a more permanent solution, with the need to investigate interactions between methods to mitigate potential side effects. The project was implemented within the frameworks of IBO 2022 International Group Project.

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