應用雙極性胜肽分子來對抗神經退化性疾病

Nanoscopic insights of amphiphilic peptides against neurodegenerative diseases

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Finding an effective therapeutic regimen is an urgent demand for various neurodegenerative disorders including Huntington's disease (HD). For the difficulties in observing the dynamic aggregation and oligomerization process of mutant Huntingtin (mHtt) *in vivo*, the evaluation of potential drugs at the molecular protein level is usually restricted. By combing lifetime-based fluorescence microscopies and biophysical tools, it is showcased that a designed amphiphilic peptide, which targets the mHtt at an early stage, can perturb the oligomer assembly process nanoscopically, suppress the amyloid property of mHtt, conformationally transform the oligomers and/or aggregates of mHtt, and ameliorate mHtt-induced neurological damage and aggregation in cell and HD mouse models. It is demonstrated this amphiphilic peptide is able to transport to the brain and rescue the memory deficit through intranasal administration, indicating its targeting specificity *in vivo*. Recently, we also found the complex of negatively-charged amphiphilic peptides with chitosan can suppress the mHtt inclusion body formation and reduced mHtt neuron toxicity. Conclusively, a biophotonic platform is provided to investigate the oligomerization/aggregation process in detail that offers insight into the design and effect of targeted therapeutic agents for Huntington's disease.

References

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