

The role of protein dopaminylation in Parkinson's Disease

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Dopamine and its oxidative derivatives can induce α -syn aggregation by modifying the structure of α -syn, which is one mechanism of Lewy body formation and neuron degeneration in Parkinson's disease (PD). However, whether dopamine modification on α -syn, named dopaminylation, was present in human plasma was unknown. This dissertation reports the analytical approach using high-resolution mass spectrometry technologies to accelerate understanding the role of dopaminylation in PD.

Firstly, a complete workflow was established to identify and quantify endogenous low abundance α -syn dopaminylation in plasma from patients with PD. The analysis among 88 human plasma samples from the PD group, healthy control group and disease control group (major depressive disorder) confirmed that endogenous dopaminylation of α -syn was significantly higher in PD than healthy control, suggesting its potentiality to indicate the presence and progression of neurological disorder in PD.

Secondly, a proteomic analysis was performed with the same set of plasma samples. As a result, some proteins related to well-known PD mechanisms/pathways are dopaminylated at different levels compared to the healthy control group. These proteins' dopaminylation indicates the oxidative stress in PD. This result opens a new perspective on PD's biochemical mechanism study and helps to find new protein participators.

In the third part of this thesis, we developed the extraction, enrichment, purification and analysis of extracellular vesicles / exosome from brain tissue based on the our platform of the proteomic analysis using mass spectrometry. This method was applied on a TGR5 mice model and revealed the difference of the proteomic profiles in TGR5 gene knockout / active group. The developed method lays a foundation for studying the biochemical mechanism of PD in the central nervous system: an extracellular vesicle proteomic analysis with post-mortem brain tissue from patients with PD.

Jury:

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