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## Statistical Investigation on the Occurrence of **Liquid-Liquid Phase Separation in Proteins Involved in Neurodegenerative Proteins**

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## Abstract

Neurodegenerative diseases are among the most prevalent health issues worldwide. Among them, Alzheimer's is known to rank as the 6th leading cause of death and exhibits heterogeneous mechanisms. According to research, neurodegenerative diseases are more common among older people. Protein aggregation is a common feature among them, forming in the brains of affected patients. Liquid-liquid phase separation is an important pathway that plays a crucial role in the formation of membraneless organelles and fibrils. Molecular studies suggest that non-covalent interactions are crucial for the creation of these organelles. The amino acid sequence or content can shed light on the interactions leading to the formation of membraneless organelles. Therefore, bioinformatics methods (e.g., data mining) can reveal amino acid content and sequence-mediated phase separation in neurodegenerative diseases. In this work, we have investigated the effects of occurrence of specific amino acids (content) or specific nearest neighbor (sequence) in neurodegenerative peptides and proteins. We have analyzed sequence-based statistics investigating the





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occurrence of LLPS in the LLPSv2 database, and on neurodegenerative peptides and proteins. The calculations were based on statistical methodologie (e.g., Paired T-test). Our results indicated that specific AACs (amino acid compositions) such as A, L, F, and Y, and PCs (peptide compositions) such as KK, VG, GV, and YY were important in the occurrence of LLPS. We concluded that hydrophobic, hydrophilic, and electrostatic interactions were the most important physicochemical properties and were frequently involved in the interactions that play crucial roles in the occurrence of LLPS.

**Keywords**: Bioinformatics, phase separation, aggregation, amino acid content and sequence

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