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Putting a spin on it: amyloid aggregation from oligomers to fibrils

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Stellingen

Behorend bij het proefschrift

Putting a Spin on it: Amyloid Aggregation from Oligomers to Fibrils

1. A glycine amino acid added to the TOAC spin label at the N-terminus of the T0A β peptide reduces the local mobility and enhances the sensitivity of EPR to the size of the aggregates. [**Chapter 3 + Chapter 6**]
2. While the TOAC spin label is better than the MTSL spin label to determine the size of aggregates of smaller peptides, the high local mobility of MTSL helps to differentiate oligomers from fibrils in systems with a large molecular weight. [**Chapter 4 + 6**]
3. The use of a thioether linked spin label can prevent the formation of free spin label during the aggregation of spin-labeled α -synuclein. [**Chapter 4**]
[J. Eralles, M. Lorenzi, R. Lebrun, A. Fournel, E. Etienne, C. Courcelle, B. Guigliarelli, B. Gontero, V. Belle, *Biochemistry* **2009**, 48, 6034–6040].
4. The enhanced ThioT activity of equimolar or weakly sub-stoichiometric mixtures of CP-2 with Amyloid Beta, suggesting fibril formation, hints to the possible accumulation of fibrils in the brain as a side effect of a CP-2 based drug. [**Chapter 6**]
[M. Chemerovski-Glikman, M. Richman, S. Rahimipour, *Tetrahedron* **2014**, 70, 7639–7644].
5. The bioresistant nature of the M-TETPO nitroxide spin label makes it a possible candidate to study *in-cell* aggregation of amyloids.
[G. Karthikeyan, A. Bonucci, G. Casano, G. Gerbaud, S. Abel, V. Thomé, L. Kodjabachian, A. Magalon, B. Guigliarelli, V. Belle, et al., *Angew. Chemie - Int. Ed.* **2018**, 57, 1366–1370].
6. The cross- α amyloid fibrils, composed entirely of α -helices, are ideally suited to be characterized with a TOAC spin label by cw EPR.
[Y. Engelberg, M. Landau, *bioRxiv* **2020**, 37, 2020.02.04.933432].

7. Site-directed spin labeling of T4Lysozyme with Gd(III) paramagnetic centers *in vivo*, using the method of Widder et al., would remove all doubts about the protein's position within the cell and could improve the concentration of spin-labeled protein in the cellular environment.
[P. Widder, J. Schuck, D. Summerer, M. Drescher, *Phys. Chem. Chem. Phys.* **2020**, 22, 4875–4879].
8. Player versus player competition would increase the interest of students for the ALCHEMIST video game developed to teach chemistry.
[A. Annaggar, R. Tiemann, *ChemRxiv* **2019**].
9. Quarantine is a blessing if you have a passion for reading books.