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AVVISO DI SEMINARIO

Il Prof. Marco van de Weert

Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen.

il giorno Lunedi 11/06/2018 alle ore 14 :30
Nell'Aula seminari del Dipartimento di Scienze e Tecnologie Chimiche

Terrà un seminario dal titolo:

Aggregation of therapeutic peptides and proteins – a multifactorial challenge.

Proponente; Prof. Stella

Aggregation of therapeutic peptides and proteins – a multifactorial challenge

Therapeutic peptides and proteins are usually administered by injection or infusion. This invasive administration puts major restrictions on the content of the fluids that are injected/infused. For example, large particles (>25 µm) may block capillaries, and thus only very small numbers are allowed in any product. Recent years have also seen an increasing focus on and concern about particles smaller than 25 µm, especially when these consist of peptide/protein aggregates. These aggregates appear to increase the risk of developing an immune response against the therapeutic peptide/protein, with potential fatal consequences. Unfortunately, it is almost impossible to prevent the formation of peptide or protein aggregates, as aggregation is often thermodynamically more favorable than folding. Since the driving forces are essentially the same, whereas predictability is not, aggregation may be considered the ugly twin of the protein folding problem.

Our research spans from obtaining a fundamental insight into protein aggregation processes, in particular fibrillation, to formulation approaches to prevent such aggregation, with focus on therapeutic peptides and proteins. This presentation will highlight our attempts to prevent the aggregation of peptides and proteins, and highlight some unresolved mysteries for a folded protein (insulin), a natively unfolded protein (alpha-synuclein) and a peptide (carbetocin).

References

1. U.B. Høgstedt, J. Østergaard, T. Weiss, H. Sjögren, and M. van de Weert, 2018. Manipulating aggregation behaviour of the uncharged peptide carbetocin. *J. Pharm. Sci.* 107:838-847
2. U.B. Høgstedt, G. Schwach, M. van de Weert, and J. Østergaard, 2016. Taylor Dispersion Analysis as a promising tool for assessment of peptide-peptide interactions. *Eur. J. Pharm. Sci.* **93**:21-28
3. E.S. Lobbens, L. Breydo, T. Skamris, B. Vestergaard, A.K. Jäger, L. Jorgensen, V. Uversky, and M. van de Weert, 2016. Mechanistic study of the inhibitory activity of Geum urbanum extract against alpha-synuclein fibrillation. *Biochim. Biophys. Acta* **1864**:1160-1169
4. E.S. Lobbens, V. Foderà, N.T. Nyberg, K. Andersen, A.K. Jäger, L. Jorgensen, and M. van de Weert, 2016. The inhibitory effect of natural products on protein fibrillation may be caused by degradation products – a study using aloin and insulin. *PLoS One* **11**:e0149148
5. B. Vestergaard, M. Groenning, M. Roessle, J.S. Kastrup, M. van de Weert, J.M. Flink, S. Frokjaer, M. Gajhede, and D.I. Svergun, 2007. A helical structural nucleus is the primary elongating unit of insulin amyloid fibrils. *PLoS Biol.* **5**(5):e134

Curriculum Vitae Marco van de Weert

Marco van de Weert was born in 1973 in Scherpenzeel, the Netherlands. He currently is an Associate Professor at the Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark.

Marco received his MSc in Chemistry from Utrecht University in 1996. A PhD in Pharmaceutical Sciences was awarded in 2001 from the same university for his work on the structural integrity of pharmaceutical proteins in polymeric matrices. During his PhD he also spent three months at Genentech, in South San Francisco (USA).

After his PhD he briefly worked as a Junior Assistant Professor at the Utrecht Institute for Pharmaceutical Sciences at Utrecht University. Thereafter he moved to Copenhagen, Denmark, as an Alfred Benzon Research Fellow from 2001-2004, subsequently became an Assistant Professor, and took up his current position in 2006.

Marco's research is primarily focused on the physical instability of therapeutic peptides and proteins, in particular their aggregation, the development of analytical tools to measure this instability, and formulation approaches to minimize instability. His work has resulted in ca. 80 scientific papers and 10 book chapters, which have been cited > 4000 times. He has been the main supervisor of 7 PhD students, and co-supervisor of another 11. He is a member of the Editorial Board of the Journal of Pharmaceutical Sciences and the Journal of Molecular Structure.

Selected publications

B. Vestergaard, M. Groenning, M. Roessle, J.S. Kastrup, M. van de Weert, J.M. Flink, S. Frokjaer, M. Gajhede, D.I. Svergun; *A helical structural nucleus is the primary elongating unit of insulin amyloid fibrils*. **PLoS Biol.** (2007) 5(5):e134

U.B. Høgstedt, J. Østergaard, T. Weiss, H. Sjögren, M. van de Weert; *Manipulating aggregation behaviour of the uncharged peptide carbetocin*. **J. Pharm. Sci.** 107 (2018) 838-847

U.B. Høgstedt, G. Schwach, M. van de Weert, J. Østergaard; *Taylor Dispersion Analysis as a promising tool for assessment of peptide-peptide interactions*. **Eur. J. Pharm. Sci.** 93 (2016) 21-28

E.S. Lobbens, L. Breydo, T. Skamris, B. Vestergaard, A.K. Jäger, L. Jorgensen, V. Uversky, M. van de Weert; *Mechanistic study of the inhibitory activity of Geum urbanum extract against alpha-synuclein fibrillation.* **Biochim. Biophys. Acta** 1864 (2016) 1160-1169

S. Hedegaard, M. Cárdenas, R. Barker, L. Jorgensen, M. van de Weert; *Lipidation effect on the associated fibrillation of the model protein insulin at hydrophobic surfaces*. **Langmuir** 32 (2016) 7241-7249