ESF – Short Visit Grant - REPORT

Visits 27th July - 6th August of Joachim Rädler at UCD

Project: Investigating protein fibrillation in the presence of nanoparticles, using Fluorescence Correlation Spectroscopy.

Purpose of the visits

Protein fibrillation in the presence of nanoparticles is a key issue in nanotoxicilogy. We investigate the aggregation of a-beta peptide using Fluorescence Correlation Spectroscopy. The project is carried out in collaboration with Kenneth Dawson, Fiona Quinlan-Pluck and Dominic Walsh at UCD and Jennifer McManus at Maynooth university. The short visits was used for discussion to establish the framework, experimental conditions and data analysis for this novel approach. Experiments on sample preparation, biochemical modification and particle characterization will be carried out in Dublin, while FCS measurements are carried out in my lab in Munich.

Achievements

Alexa-labeled Abeta was prepared and characterized for FCS experiments. In previous work we have used the ThT assay in combination with FCS. These data were evaluated at UCD and showed general agreement of the ThT assay and the FCS diffusion data. In general Abeta aggregates in the presence of ThT label. Nanoparticles seem to accelerate this process. However, no clear evidence of coincidence of Abeta and nanoparticle signal was found. This limits our interpretation of the nucleation scenario. The key question for this project is to clarify, if Abeta adsorbs to nanoparticles prior to aggregation and if the adsorbed fraction triggers the aggregation kinetics. We developed a strategy to use covalently Alexa-labeled Abeta for further FCS studies. We identified fluorescently labeled nanoparticles that would we suitable for cross-correlation studies.
Jennifer McManus and Fiona Quinlan-Pluck will travel to Munich to continue the FCS experiments. Our approach should allow to detect Abeta aggregation also in serum, i.e. in clinically relevant body fluids. This would be first time that FCS would be used to study the interaction of NP and beta-amyloid in complex body fluids, which should reflect the in-vivo situation of protein corona reliably.