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Secondary Structural Changes of FUS-LC induced with Phase-Separation observed by VUV-CD

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Aggregation of the RNA-binding protein FUS (Fused in Sarcoma) has been implicated in neurodegenerative diseases such as ALS (amyotrophic lateral sclerosis) and FTD (frontotemporal dementia). The low-complexity domain of the FUS (FUS-LC) mediated liquid-liquid phase separation (LLPS), but the structural mechanism is not known in detail. To address the revealing mechanism, we examined the spectroscopic study using VUV-CD measurement, which can analyze the secondary structure of the proteins.

CD measurements were performed at BL12 VUV-CD station in HiSOR. CD spectra were measured between 185 and 260 nm. The temperature of the samples was controlled from room temperature to 5°C to obtain the LLPS of the FUS LC.

The CD spectrum obtained by measuring at room temperature has a prominent peak at 195 nm and a small shoulder peak near 220 nm. This shows that the major structure is a random coil since the spectrum was similar to that of STI, which is mainly an unordered structure. This result is consistent with that obtained from NMR measurement. The peak intensity around 195 nm decreased by cooling the sample temperature.

The reasons for the obtained spectral changes are as follows; 1) LLPS showed secondary structural changes, 2) LLPS made an effect to decreasing the transmission light intensity by scattering of suspension. We examine the measurement by changing the relative distance between the cell and the photo-multiplier detector. This may clarify the contribution of the scattering effect on the obtained spectrum.