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A single molecule perspective on the role of biomolecular condensation in FUS mediated DNA damage repair

Biomolecular condensation (BC) has recently been found to govern the spatial and temporal organization of the intracellular space with respect to various processes. FUS (Fused in Sarcoma) is an intrinsically disordered protein that forms condensates at sites of DNA damage in vivo and liquid-like droplets that harden over time in vitro. A detailed picture of the assembly process of FUS based repair compartments at DNA damage sites is, however, still missing. We study the role of BC in the interaction of FUS and DNA on the single molecule level using optical tweezers-based micromanipulation combined with confocal fluorescence imaging.
We found that FUS shows different binding modes with DNA and forms dynamic condensates with free single stranded DNA at DNA nicks. The material properties and composition of these condensates depend on the FUS concentration and the number of incorporated nucleotides.
We propose that dynamic repair compartments formed by BC might not only facilitate recruitment of downstream repair factors, but also prevent disassembly of DNA fragments and promote local concentration of damage sites and thus assist the efficient assembly and functionality of the DNA damage repair machinery.

Primary author(s) : Mr RENGER, Roman (MPI-CBG)

Co-author(s) : Dr MORIN, José Lantero (MPI-CBG); Prof. GRILL, Stephan W. (MPI-CBG)

Presenter(s) : Mr RENGER, Roman (MPI-CBG)

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