Elia Moarbess[1, 2], Caroline Clerte[2], Jihane Basbous[1], Christine Doucet[2], Angelos Constantinou[1] and Pierre-Emmanuel Milhiet[2].

1. Institut de Génétique Humaine, Université de Montpellier - CNRS, Montpellier, France

2. Centre de Biologie Structurale (CBS), Université de Montpellier, CNRS, INSERM, Montpellier, France.

The ATR/Chk1 signaling pathway is crucial for the cellular response to DNA lesions that block the progression of replication forks. ATR/Chk1 signaling promotes DNA repair mechanisms in coordination with cell physiological processes such as DNA replication, transcription, and cell cycle progression. The main activator of ATR in S phase is topoisomerase IIB-binding protein (TopBP1), a multivalent protein scaffold that promotes the assembly of nuclear condensates. TopBP1 condensation triggers ATR/Chk1 signaling via an amplification mechanism. Our objective is to reveal the underlying structure and the biophysical properties of TopBP1 condensates. While TopBP1 condensates appear as spherical nuclear foci by conventional microscopy, super-resolution STED microscopy reveals that TopBP1 foci consist in tight cluster of nanometer-sized condensates. We are using single-particle tracking (SPT) in live cells to understand the nanoscale organization and dynamics of TopBP1 molecules within condensates induced by cellular treatment with inhibitors of topoisomerase 1. This knowledge will be essential to understand the mechanism of assembly and the functions of TopBP1 condensates induced by DNA damage.