Chromatin and Chromosome dynamics during DNA Double Strand break repair

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DNA double-strand breaks (DSBs) are highly toxic lesions that are rapidly repaired by two main pathways, namely Homologous Recombination (HR) and Non Homologous End Joining (NHEJ). Using a cell line, called DIvA (for DSB Inducible via AsiSI), where multiples breaks can be induced at annotated positions throughout the human genome, we previously reported that DSBs induced in transcriptionally active genes are channeled to HR during G2, thanks to a chromatin dependent signaling, while DSB occurring in intergenic regions rather undergo NHEJ. Using Capture Hi-C and super resolution microscopy, we further reported that these DSBs induced in active genes undergo clustering in an ATM dependent manner and mostly during G1. Notably, clustering coincides with delayed repair in G1. Collectively our data suggest that when damaged, transcriptionally active units adopt a very peculiar behavior, being repaired by HR in G2 and left unrepaired and clustered in G1. More recently, using this cell line, we have investigated, using ChIP-seq and Hi-C, 4C-seq the chromatin structure assembled around DSBs. This allowed us to unveil basic principles of chromatin structure dynamics occurring at DSBs and to identify Topologically Associating Domains (TADs) as functional units during DSB repair.