

## ***Landscape of double-stranded DNA breaks in human genome and its correlation with sequence motifs and DNA bendability***

We have developed a genome-wide approach to map DNA double-strand breaks (DSBs) at nucleotide resolution by a method we termed BLESS (direct *in situ* breaks labeling, enrichment on streptavidin and next-generation sequencing). We validated and tested BLESS using human and mouse cells and different DSBs-inducing agents and sequencing platforms. Our method is suitable for genome-wide mapping of DSBs in various cells and experimental conditions, with a specificity and resolution unachievable by current techniques. We characterized the genomic landscape of sensitivity to replication stress in human cells, and we identified >2,000 nonuniformly distributed aphidicolin-sensitive regions (ASRs) overrepresented in genes and enriched in satellite repeats. ASRs were also enriched in regions rearranged in human cancers, with many cancer-associated genes exhibiting high sensitivity to replication stress. This exciting result contributes to understanding why some genes are more often mutated in cancers. Our data also shows that double-stranded breaks occur more often in transcribed regions, thus supporting the hypothesis that collisions between transcription and replication machineries contribute substantially to DNA double-breaks formation. We are currently modeling *in silico* movements and collisions of these complexes and will verify the computational predictions experimentally.

### **Reference:**

N. Crosetto, A. Mitra, M. J. Silva, M. Bienko, N. Dojer, Q. Wang, E. Karaca, R. Chiarle, M. Skrzypczak, K. Ginalski, P. Pasero, **M. Rowicka** (a corresponding author) & Ivan Dikic: Nucleotide-resolution DNA double-strand break mapping by next-generation sequencing, ***Nature Methods***, in press.