Physiological DNA strand breaks

The stability of the genome is secured by regulating the balance between the emergence and repair of errors in it. In the course of their repair, DNA double-strand breaks may lead to chromosome translocations and eventually to cancer. Whether such breaks occur randomly or primarily at sites made vulnerable by physiological functions is an important, unresolved question. One of the research groups of the Department of Biophysics and Cell Biology at the Faculty of Medicine of the University of Debrecen, in local as well as international collaboration, has recently described (Hegedüs et al., Nucleic Acids Res. 2018 Nov 16;46(20):10649-10668) endogenous, promoter-proximal single-strand discontinuities in the genome of healthy, non-dividing yeast cells. Based on their observations the authors assume that these transient, physiological single-strand breaks contribute to the formation of the pathological double-strand breaks. Several decades of research conducted by the group has prompted them to hypothesize that such vulnerable sites are present also in the DNA of human cells. The experience obtained in the yeast model system and the novel methods developed pave the way for further efforts to understand the mechanism of DNA break generation, and their role in gene regulation, in human cells.

Figures below: The individual DNA molecules of yeast chromosomes underwent double-strand breakage exactly where the single-strand breaks got labeled before DNA isolation. These proved to be primarily promoter (TSS) regions, what was confirmed also by the presence of initiating RNA polymerase in the chromatin fragments immobilized on microbeads via the label. Single-strand breaks were identified also at discrete sites (a-i) within the rDNA units.