Contribution ID : **24** Type : **not specified**

8-oxodG accumulation within super-enhancers marks fragile CTCF-mediated chromatin loops.

lunedì 28 febbraio 2022 12:40 (10)

8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxodG), a major product of the DNA oxidization process, has been proposed to have an epigenetic function in gene regulation and has been associated with genome instability. NGS-based methodologies are contributing to the characterization of the 8-oxodG role in many genome-related functions. However, the number of studies addressing the 8-oxodG epigenetic role at a genomic level is still low and the mechanisms controlling genomic 8-oxodG accumulation/maintenance have not yet been fully characterized. In this study, we report the identification and the characterization of a set of enhancer regions accumulating 8-oxodG in human epithelial cells. We found that these oxidized enhancers are mainly super-enhancers and are associated with bidirectional-transcribed enhancer RNAs and DNA Damage Response activation. Moreover, using ChIA-PET and HiC data, we identified specific CTCF-mediated chromatin loops in which the oxidized enhancer and promoter regions physically associate. Oxidized enhancers and their associated chromatin loops accumulate endogenous double-strand breaks which are in turn repaired by NHEJ pathway through a transcription-dependent mechanism. Our work provides novel mechanistic insights on the intrinsic fragility of chromatin loops containing oxidized enhancers-promoters pairs and suggests that 8-oxodG accumulation in these latter occurs in a transcription-dependent manner.

Department

Department of Molecular Medicine and Medical Biotechnologies, University of Naples ‘Federico II’, Naples, Italy

Primary author(s) : Dr. GIOVANNI, Scala (1Department of Biology, University of Naples ‘Federico II’, Naples, Italy); Dr. FRANCESCA, Gorini (Department of Molecular Medicine and Medical Biotechnologies, University of Naples ‘Federico II’, Naples, Italy); Dr. SUSANNA, Ambrosio (1Department of Biology, University of Naples ‘Federico II’, Naples, Italy); Dr. ANDREA MARIA, Chiariello (Department of Physics, University of Naples Federico II, and INFN, Naples, Italy); Prof. MARIO, Nicodemi; Prof. LUIGI, Lania (Department of Molecular Medicine and Medical Biotechnologies, University of Naples ‘Federico II’, Naples, Italy); Prof. BARBARA , Majello (Department of Biology, University of Naples ‘Federico II’, Naples, Italy); Prof. STEFANO, Amente (Department of Molecular Medicine and Medical Biotechnologies, University of Naples ‘Federico II’, Naples, Italy)

Presenter(s) : Prof. STEFANO, Amente (Department of Molecular Medicine and Medical Biotechnologies, University of Naples ‘Federico II’, Naples, Italy)