



## Project Proposal

### Title

**Systems biology modelling of the role of DNA damage repair and autophagy in cancer**

### Project Description

Our research team has a long-standing tradition in Molecular Genetics and its applications to Molecular Oncology. Currently, we are implementing genomic strategies and cellular methodologies as diagnostic tools to correlate DNA damage lesions and cell death, in particular autophagy and senescence. Specifically, the research team uses cellular systems and omics approaches to analyze the intertwined relationship between autophagy and DNA damage repair pathways. Systems biology modelling of the role of autophagy and DNA damage repair in cancer resistance to therapies will be used to assess the clinical relevance of autophagy in resistance to therapy by in vivo tumor phenotyping experiments, for the identification of effectors candidates and biomarkers.

The identification of specific tumor types and biomarkers that facilitate our understanding and rationale of the intertwined relationship between autophagy and DNA Damage, is expected to produce novel, practical outputs of future benefit to patients with difficult-to-treat malignancies.

The ideal candidate should have a background in data analysis, machine learning techniques along with interest and/or knowledge of molecular cellular methodologies.

She/He will work within collaborations with our current partners in Italy, EU and USA.

### Supervisor(s), Lab/Group details, other additional info.

Barbara Majello, University of Naples "Federico II"

web: <http://www.dipartimentodibiologia.unina.it/personale/barbara-majello/>

Additional information is available via email upon request

### Funding

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### References

1. The genomic landscape of 8-oxodG reveals enrichment at specific inherently fragile promoters. Gorini F, Scala G, Di Palo G, Dellino GI, Cocozza S, Pelicci PG, Lania L, Majello B, Amente S. **Nucleic Acids Res.** 2020; 48:4309-4324. doi: 10.1093/nar/gkaa175.
2. Knowledge Generation with Rule Induction in Cancer Omics. Scala G, Federico A, Fortino V, Greco D, Majello B. **Int J Mol Sci.** 2019; 21:18. doi: 10.3390/ijms21010018.
3. Inhibition of lysine-specific demethylase LSD1 induces senescence in Glioblastoma cells through a HIF-1 $\alpha$ -dependent pathway. Saccà CD, Gorini F, Ambrosio S, Amente S, Faicchia D, Matarese G, Lania L, Majello B. **Biochim Biophys Acta Gene Regul Mech.** 2019 1862:535-546. doi: 10.1016/j.bbagr.2019.03.004.



4. Expanding the Role of the Histone Lysine-Specific Demethylase LSD1 in Cancer. Majello B, Gorini F, Saccà CD, Amente S. **Cancers**. 2019;11:324. doi: 10.3390/cancers11030324.
5. Genome-wide mapping of 8-oxo-7,8-dihydro-2'-deoxyguanosine reveals accumulation of oxidatively-generated damage at DNA replication origins within transcribed long genes of mammalian cells. Amente S, Di Palo G, Scala G, Castrignanò T, Gorini F, Cocozza S, Moresano A, Pucci P, Ma B, Stepanov I, Lania L, Pelicci PG, Dellino GI, Majello B. **Nucleic Acids Res**. 2019; 47:221-236. doi: 10.1093/nar/gky1152.
6. Histone methyl-transferases and demethylases in the autophagy regulatory network: the emerging role of KDM1A/LSD1 demethylase. Ambrosio S, Ballabio A, Majello B. **Autophagy**. 2019; 12:187-196. doi: 10.1080/15548627.2018.1520546
7. Targeting Histone Demethylase LSD1/KDM1a in Neurodegenerative Diseases. Ambrosio S, Majello B. **J Exp Neurosci**. 2018; 12: 1179069518765743. doi: 10.1177/1179069518765743.
8. Lysine-specific demethylase LSD1 regulates autophagy in neuroblastoma through SESN2-dependent pathway. Ambrosio S, Saccà CD, Amente S, Paladino S, Lania L, Majello B. **Oncogene**. 2017; 36:6701-6711. doi: 10.1038/onc.2017.267
9. Epigenetic regulation of epithelial to mesenchymal transition by the Lysine-specific demethylase LSD1/KDM1A. Ambrosio S, Saccà CD, Majello B. **Biochim Biophys Acta Gene Regul Mech**. 2017; 1860:905-910. doi: 10.1016/j.bbagr.2017.07.001