

Prize for Best DBMR Publication 2023

The prize is awarded in recognition of an outstanding publication published during the 2023 calendar year led by an investigator from the DBMR.

Best DBMR Publication 2023

At the DBMR Day of BioMedical Research 2023 on July 3 2024, it was announced that the winner of the Best DBMR Publication 2023 was:



Dr. Roberta Esposito

Department for BioMedical Research
Translational Cancer Research

For the paper *Tumour mutations in long noncoding RNAs enhance cell fitness*, *Nature Communications* 14, 3342 (2023).

DOI: [10.1038/s41467-023-39160-7](https://doi.org/10.1038/s41467-023-39160-7)

Traditionally, cancer-promoting mutations, known as 'driver' mutations, have been predominantly studied within protein-coding regions of the genome. This study pioneers the identification of driver mutations within the "dark genome", particularly impacting the activity of long non-coding RNAs (lncRNAs). Through the development of a software pipeline, ExInAtoR2, the authors embarked on a comprehensive analysis of millions of tumor mutations, scrutinizing 2583 primary tumors and 3527 metastatic tumors. The results unveiled 54 candidate 'driver' lncRNAs. Among these, the lncRNA NEAT1 emerged as a prominent gene. Prior studies noted a dense concentration of mutations at the NEAT1 locus, often dismissed as inconsequential noise. However, by employing *in cellulo* (i.e. in living cells) mutagenesis with CRISPR-Cas9, the authors demonstrated NEAT1 transformative potential, reproducibly inducing increased cell proliferation across various cellular contexts and in an *in vivo* model. Delving deeper into NEAT1's molecular landscape, this study uncovered its intricate role in orchestrating the assembly of

ribonucleoprotein paraspeckle organelles. Tumor mutations within NEAT1 disrupt critical protein interactions, reshaping the cellular landscape and promoting paraspeckle formation and cell growth. This research shows how somatic tumor mutations harness the power of lncRNAs to drive cellular fitness, and it is the first experimental evidence that mutations in lncRNAs can drive cancer. This mechanistic insight lays the groundwork for future exploration, offering a roadmap to decipher the mechanisms of driver lncRNAs in cancer.

The DBMR congratulates Dr. Esposito for the award and all co-authors for the excellent publication!