

# **DBMR Prize for Innovative Research Idea 2024**

## **Establishing the minor spliceosome as an innovative therapeutic target for breast cancer**

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Dysregulated splicing is a well-recognized cancer hallmark, as such the spliceosome has emerged as a new frontier for cancer therapeutics. In a recent study, I found that cancer specifically employs a specialized spliceosome called the minor spliceosome (MiS) to splice the genes that drive cancer hallmarks and to increase cell plasticity. While I extensively established this concept in prostate cancer (PCa), my preliminary data strongly suggests that overactivity of the MiS is a broadly applicable oncogenic principle with potential implications for breast cancer (BCa), another prevalent and hormone-dependent tumor type. Additionally, my preliminary data indicates that blocking MiS activity induces a BRCAness phenotype in BCa and thus sensitizes towards DNA targeting treatments such as radiation or PARP inhibitors in BCa. Nevertheless, our understanding of how minor intron splicing contributes to BCa biology, heterogeneity and complexity of resistance is still lacking. Therefore, I propose to leverage my expertise in cancer biology and MiS to systematically study the role of minor intron splicing in BCa and to ultimately establish the MiS as an innovative vulnerability in genetically distinct molecular BCa subtypes that could be exploited as mono or combination therapy.