# P-bodies regulate cell homeostasis during DNA damage via epitrascriptomic mechanisms

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## ABSTRACT

DNA damage poses a significant threat to cellular health, prompting the activation of a complex DNA Damage Response (DDR) pathway. Traditionally, DDR research has focused on protein-centric pathways involving DNA damage sensors and signal transducers. However, recent evidence indicates that RNA also plays a crucial role in DDR, functioning as a template, scaffold, and regulator during DNA repair. Despite this, the precise mechanisms by which RNA influences DDR remain largely unexplored. Recent findings suggest that DNA damage induces epitranscriptomic modifications in newly synthesized transcripts, introducing an additional layer of regulation in the RNA-dependent DDR [1, 2].

In this project, we investigate the regulatory roles of RNA modifications, with a particular focus on $m^6A$ methylation, in response to DNA damage. We aim to understand whether these modifications influence the fate of transcripts as they transition from the nucleus to the cytoplasm. Interestingly, $m^6A$ modification in mRNAs is proposed to promote recruitment in cytoplasmic, membrane-free ribonucleoprotein aggregates, called P-bodies. These are primarily composed of regulatory mRNAs and RNA-binding proteins and play a crucial role in determining the fate of associated RNAs, either by degrading them or facilitating their translation.

Our findings reveal a significant dependency between DNA damage and the presence of p-bodies, mediated through both the DNA damage response (DDR) and methyltransferase activity. Additionally, we observe that methylated transcripts, which encode DDR and repair-related proteins, accumulate in P-bodies in response to DNA damage. This accumulation facilitates their selective translation, thus influencing cell fate and homeostasis.

### REFERENCES

1. Xiang, Y. et al. (2017) RNA m(6)A methylation regulates the ultraviolet-induced DNA damage response. Nature 543 (7646), 573-576.
2. Kalamara, V. and Garinis, G.A. (2024) The epitranscriptome: reshaping the DNA damage response. Trends Cell Biol.