Dipartimento di
Farmacia
Dipartimento di Eccellenza
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UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

PROPOSTA PROGETTUALE
DOTTORATO IN *RNA Therapeutics and gene therapy*
CICLO XLI*

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Co-tutor: Anna Di Porzio

PROJECT TITLE
Role of DNA G-quadruplex structures in the regulation of gene expression: molecular mechanisms and therapeutic implications

Project description (max 300 words)
G-quadruplexes (G4s) are guanine-rich secondary structures of DNA that form in specific genomic regions, particularly within gene promoters and telomeres (1). Recent studies have shown that G4s can modulate gene expression both positively and negatively, acting as dynamic regulatory elements (2, 3). However, the molecular mechanisms through which these structures influence transcription remain largely unexplored.
This research project aims to systematically investigate the role of G4 structures in gene regulation. In the initial phase, the genome-wide distribution of G4s in the human genome will be mapped using advanced chromatin immunoprecipitation techniques such as ChIP-seq and Cut&Tag, employing G4-specific antibodies and, if necessary, developing novel G4-specific nanobodies. The goal is to identify promoter regions that are particularly enriched in these structures.
Subsequently, the impact of G4s on transcriptional activity will be analyzed through reporter gene assays, to assess how the formation or destabilization of G4s affects the expression of specific target genes. Finally, the project will explore the potential therapeutic implications of modulating G4 structures using small molecules capable of stabilizing or destabilizing them, with the aim of evaluating their effects on the expression of oncogenes and genes implicated in neurodegenerative diseases.
By integrating molecular biology, functional genomics, and bioinformatic analysis, this study seeks to advance our understanding of the regulatory role of G-quadruplex structures in gene expression and to evaluate their potential as therapeutic targets in biomedical research.

REFERENCES
(1) V. S. Chambers, *Nat. Biotechnol*, 2015, DOI: 10.1038/nbt.3295;
(2) I. Esain-Garcia, *PNAS*, 2024, DOI: 10.1073/pnas.2320240121;
(3) C. Broxson, *Biochemistry*, 2011, DOI: 10.1021/bi2002136.

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***Per il dottorato *in RNA Therapeutics and gene therapy* selezionare anche una delle seguenti aree tematiche:**

- ☒ **Mechanisms of Diseases and Drug Target Identification**
- ☐ **Design and Delivery of New Gene Therapy and RNA-Based Medicines**
- ☐ **Validation and Safety In Preclinical and Clinical Studies**

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