PROPOSTA PROGETTUALE
DOTTORATO IN RNA THERAPEUTICS AND GENE THERAPY
CICLO XLI

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PROJECT TITLE Mechanisms of interactions between α-sinuclein and hDAT.

Project description (max 300 words**)**

Parkinson's disease (PD) is a neurodegenerative disorder marked by the gradual degeneration of dopaminergic neurons in the *substantia nigra pars compacta*. Extensive research highlights the significant role of the protein α-synuclein (αS) in the development of PD. Normally expressed throughout the brain, αS is thought to be involved in the vesicular release of neurotransmitters. In the pathological context of PD, however, an increase in the expression levels of αS or alterations in its conformational properties result in the formation of intraneuronal inclusions, Lewy bodies, in conjunction with the progressive impairment and loss of dopamine (DA) neurons. Recent research indicates that αS may interact with the human dopamine active transporter (hDAT), altering its function and contributing to both early and late symptoms of the disease, as well as related histopathological changes. This study aims to characterise in detail the interaction between αS and hDAT both *in vitro* and *in vivo*. By examining the functional and pathological significance of this protein-protein interaction, we aim to identify a new drug target that could lead to innovative therapeutic approaches for treating PD.

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