Ottava Giornata della Ricerca della Svizzera Italiana
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Modulo per la sottomissione abstract ricerca di LABORATORIO

Titolo (massimo **15 parole**)

Study of structural and functional biomolecular interactions of neurodegeneration-associated proteins in the living cell

Autori (cognome e iniziali, es: Grassi L.)

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Testo (massimo **250 parole**, preferibilmente in italiano (accettato anche in inglese), suddiviso in Introduzione, ***Metodi***, ***Risultati***, ***Conclusioni*** e ***Finanziamento***

Introduction: Protein aggregation characterizes pathological conditions associated to neurodegenerative disorders. Oligomeric forms of TDP-43, a protein implicated in FTD/ALS, are crucial for its physiological function; whereas their destabilization leads to pathological inclusions. We investigated the molecular mechanisms involved in TDP-43 self-assembly in cells.

Methods: Several cellular and biochemical assays based on bi- and tri-molecular GFP fluorescence complementation (FC) were developed and implemented to quantitatively analyze TDP-43 self-assembly.

Results: Physiological TDP-43 oligomers were first detected in the cell nucleus by triFC microscope analysis. We then demonstrated that TDP-43 oligomers form through the self-assembly of the N-terminal domain and described the contribution of the six amino acids responsible for this specific interaction. Quantification was performed by cytofluorimetry using intact cells. We then validated these data by orthogonal analytical procedures (immune isolation/blotting; surface-linked immune detection) in order to biochemically characterize the reconstituted complex. Disruption of normal TDP-43 oligomerization critically compromised its normal function in RNA splicing and induced the appearance of pathological TDP-43 forms. A large number of negative and positive controls were essential for granting the accuracy of the obtained results. These data were included in two publications (Afroz et al. NatCommun 2017;8:45; Foglieni et al. SciRep 2017;7:14013).

Conclusions: In this study, we highlight the versatility of bi/triFC as a method to characterize and quantify protein-protein interactions as well as to obtain structural information of protein assemblies in living cells.

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Visto superiore (prego indicare Nome e Cognome del superiore)

Paolo Paganetti

Criteri per sottomissione Abstract:
NO Case report
NO Abstract senza nessun risultato
VISTO da un superiore

Invio Abstract