9° Giornata della Ricerca della Svizzera Italiana
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Modulo per la sottomissione abstract ricerca di LABORATORIO

Titolo (massimo **15 parole**)

Analysis of Tau-KO cells reveals a new role of Tau protein in modulating cell death

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***

Age-dependent neurodegenerative tauopathies are characterized by the neuronal accumulation of pathogenic forms of Tau with gain-of-cytotoxic function. Beside rare dominant hereditary forms, the reasons linking the pathogenic Tau forms and neurodegeneration remain poorly understood. One well-accepted risk factor is aging, which can also be described as a progressive accumulation of DNA damage. We studied the link between the cellular DNA damage response (DDR) and a loss-of-function of Tau.

We generated Tau-KO cells utilizing the CRISPR-Cas9 technology and analysed the DDR in the absence or presence of Tau based on cellular and biochemical assays.

Following a short treatment with Etoposide, a topoisomerase II inhibitor, the absence of Tau significantly protected the cells from DNA damage-induced cell death but increased the induction cell senescence. Analysis of the DDR allowed excluding that the absence of Tau affected DNA damage or the early DDR phases. Importantly, Tau-KO lines presented a perturbation of p53 expression during the DDR. Nutlin-3, a compound interfering with MDM2-mediated degradation of p53, restored p53 expression and partly restored cell death-induction in Tau-KO cells.

We demonstrate that Tau may represent a modifier of p53 function and a modulator of cell fate as a consequence of DNA damage. Tau may represent a molecular switch between cell death and senescence. Our data indicate a loss-of-function of Tau in protecting against cellular senescence and may improve the understanding of tauopathies whilst suggesting a role of Tau in cancer.

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Visto superiore* (prego indicare **Nome e Cognome** del superiore) ***campo obbligatorio**

Paolo PAGANETTI

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

Invio Abstract