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Modulo per la sottomissione abstract di ricerca CLINICA

Titolo (massimo **15 parole**)

Mitochondria dynamics: a key driver of cancer stem cell self-renewal

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: Mitochondria reprogramming is emerging as a key feature in human cancers promoting tumor-initiating properties, survival in hostile microenvironments and treatment resistance of cancer stem cells (CSC). Identifying pharmacologically targetable elements in this process may provide new approaches for treatment of cancer. In this study, we examined the role of dynamin-related GTPase DRP1 and its outer-mitochondrial membrane receptor, MFF, in controlling mitochondria dynamics and self-renewal of prostate CSC.
Methods: Lentiviral-encoded short hairpin RNA (shRNA) were used to deplete DRP1 and MFF and examine the effects on stem-like and bulk tumor cells in cell cultures and mouse xenografts. Dominant negative DRP1 (dnDRP1) was used to inhibit endogenous DRP1 function. Mitochondria were examined by confocal microscopy and Seahorse assays.
Results: Stable depletion of DRP1 impaired in vitro expansion of tumor-sphere forming stem-like cells, indicative of reduced self-renewal and proliferative potential of prostate CSC, whereas bulk tumor cells were minimally affected. Notably, dnDRP1 expression and MFF knockdown caused a similar selective inhibition of CSC. DRP1-depleted tumor-sphere cells exhibited altered mitochondrial dynamics along with reduced mitochondrial membrane potential and spare respiratory capacity. Impaired mitochondrial fission was associated with senescence and loss of self-renewal capability in CSC. Moreover, DRP1-depleted cancer cells grew poorly in mice and the ensuing xenografts were consistently depleted of tumor-propagating CSC.
Conclusions: Our data indicate that prostate CSC highly depend on mitochondrial fission to avoid senescence and preserve self-renewal and tumorigenic potential. Interfering with key mediators of mitochondrial fission might provide innovative approaches for treatment of prostate cancer.

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Carlo V. Catapano, Prof.

Criteri per sottomissione Abstract:
NO Case report
NO Abstract senza nessun risultato
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Invio Abstract