

Exploring the role of Fragile X Mental Retardation Protein in melanoma progression and invasiveness-related pathways in melanoma cells

Simone Carotti¹, Francesca Zalfa¹, Vincenzo Panasiti², Maria Zingariello¹, Vincenzo Roberti³, Laura Sancillo⁴, Giuseppe Perrone⁵, Rosa Alba Rana⁶, Jean-Christophe Marine⁷, Claudia Bagni⁸, Sergio Morini¹

¹ University Campus Bio-Medico of Rome, Department of Medicine, Unit of Microscopic and Ultrastructural Anatomy, Rome, Italia

² University Campus Bio-Medico of Rome, Department of Medicine, Plastic and Reconstructive Surgery Unit, Rome, Italia

³ University of Rome 'La Sapienza', Department of Dermatology, Rome, Italia

⁴ University of Chieti 'G d'Annunzio', Department of Medicine and Science of Aging, Chieti, Italia

⁵ University Campus Bio-Medico of Rome, Department of Anatomical Pathology, Rome, Italia

⁶ University of Chieti 'G d'Annunzio', Department of Medicine and Science of Aging, Rome, Italia

⁷ VIB/Center for the Biology of Disease, Laboratory for Molecular Cancer Biology, Leuven, Belgio

⁸ University of Lausanne, Department of Fundamental Neuroscience, Lausanne, Svizzera

The Fragile X Mental Retardation Protein (FMRP) is an RNA binding protein, involved in multiple steps of RNA metabolism in neurons [1]. FMRP is lacking or mutated in patients with the Fragile X syndrome (FXS), a form of inherited mental retardation. Recently it has been also demonstrated that FMRP modulates metastasis formation in breast cancer, regulating the metabolism of mRNAs involved in cancer progression [2]. But the role of this protein has never been investigated in other types of cancer. Considering the similarities existing in the embryological origin between neurons and melanocytic cells, the aim of the present study is to investigate the role of FMRP in melanoma progression. FMRP overexpression is found in melanomas characterized by high Breslow's thickness and high Clark level, suggesting an association between FMRP increased expression and metastatic phenotype in melanoma. Furthermore, a reduction of FMRP in metastatic melanoma cell lines affecting their migration, invasion and adhesion properties, is found. Next-generation sequencing in human melanoma cells revealed that FMRP regulates a large number of mRNAs involved in relevant processes of melanoma progression. These data clearly show that FMRP in melanoma, as in breast cancer, is associated with an invasive phenotype and potentially related with cancer progression, suggesting in this way possible future therapeutic targets in melanoma.

References

- [1] Zalfa et al. (2003) The fragile X syndrome protein FMRP associates with BC1 RNA and regulates the translation of specific mRNAs at synapses. *Cell*. 112(3):317-27.
- [2] Lucà et al. (2013) The fragile X protein binds mRNAs involved in cancer progression and modulates metastasis formation. *EMBO Mol Med*. Oct;5(10):1523-36.

Key words

Fragile X mental retardation protein, melanoma, tumoral invasion.