

Al collegio docenti del Dottorato in Medicina Molecolare

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Ciclo: XXXVII Tutor: Antonella Naldini

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Introduction

The tumour microenvironment (TME) is characterized by hypoxia, a condition in which malignant melanoma cells increase their migratory and invasion capabilities. Carbonic anhydrases (CAs) are a family of metalloenzymes, which are involved in pH regulation, cell survival and migration. The isoforms IX and XII are overexpressed in tumours and, at the same time, embryonic developmental pathways, such as Hedgehog (Hh) pathway, are re-activated. Dendritic cells (DCs), the most potent antigen presenting cells, are exposed to hypoxia, since they are present in the TME.

Methods

Melanoma Cell lines (SK-MEL-28 and A375) were cultured in vitro and exposed to normoxia (20% O₂) and hypoxia (2% O₂); cells were treated with siRNAs targeting Hh pathway components Smoothed (SMO) and GLI1 and CAXII; Wound healing assay, Zymography, modified boyden chamber, Western Blot and qRT-PCR were performed.

Human monocyte-derived DCs were isolated from buffy coats and were exposed to normoxia and hypoxia; JC-1 assay, Western Blot and qRT-PCR were performed.

Results

We observed that the inhibition of SMO and GLI1 resulted in downregulation of CAXII expression under hypoxia, in melanoma cells lines, and, inhibition of CAXII reduce their migratory and invasion capabilities. We demonstrated that CAXII and the Hh pathway are relevant in melanoma migration and invasion.

With regard to DC, preliminary results indicate the impact of hypoxia on DC autophagy.

Seminars attended

- HypoxEU II 9/12/2021 (Gregory Cocchiaro)
- Precision Oncology in breast cancer: from biology to clinical application, 15/12/2021 - Cro Aviano
- Chromatin Immunoprecipitation (ChIP) Workshop - Led by Dr Toryn Poolman from University College London, 27/01/22
- Charles river, The Consequences of Sex Bias in Preclinical Research, 29/03/22
- IPAM2022, 3days for 3Rs, 7-14-21/02/22
- Immunoprecipitation Workshop - All about IP, 7/04/22

Conferences (Abstracts)

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Coppola F , Monaci S., Falsini A. , Aldinucci C. , Rossi D. , Filippi L., Sozzani S., Carraro F. and Naldini A. Hypoxia triggers autophagy in human monocyte-derived dendritic cells. HypoxEu live 2022, Dublin, 11/09-14/09 2022.

Falsini A. , Giuntini G., Coppola F , Monaci S. , Aldinucci C. , Naldini A. and Carraro F. Inhibition of CAMI impaired melanoma cell migration and invasion under hypoxia. HypoxEu live 2022, Dublin, 11/09-14/09 2022.

Publications

Giuntini, G, Coppola, F., Falsini A., Filippi, L, Monaci, S., Naldini, A. and Carraro, F. (2022). Role of the Hedgehog Pathway and CAXII in Controlling Melanoma Cell Migration and Invasion. Cancers 14, 4776. <https://doi.org/10.3390/cancers14194776> I F. 6,57.