Al collegio docenti del Dottorato in Medicina Molecolare

Dr.ssa Gaia Giuntini
Ciclo: XXXIV Tutor: Fabio Carraro

Introduction: Carbonic anhydrases (CAs) are a family of metalloenzymes involved in ion transport, acid-base regulation and gas exchange. The isoform IX (CAIX) and XII (CAXII) play pivotal roles in tumor cell adaptation and survival and resulted overexpressed in many cancers, such as melanoma. Moreover, their expression is triggered by hypoxia, which is known to be responsible for the cancer progression.

Aberrant activation of Hedghehog (Hh) pathway also correlates with tumorigenesis and cancer maintenance. Recent evidences have demonstrated a correlation between CAXII and Hh pathway in breast cancer; however, in malignant melanoma they have not been correlated before. The aim of this second year of PhD was focused on understanding the mechanism regulating melanoma cell line migration and invasion by targeting CAXII via either CAs inhibitors or through the inhibition of Hh pathway.

Material and methods: I performed in vitro cell cultures, vitality and proliferation assays, scratch assay, invasion assays, proteins and RNA extraction, quantitative reverse transcription PCR (qRT-PCR), Western Blots, zymography and immunofluorescence staining. Hypoxic experiments were conducted in the hypoxic Workstation INVIVO (Ruskinn).

Results: We observed that malignant melanoma motility could be impaired targeting CAXII by using both CAs or Hh pathway inhibitors, especially under hypoxia, where CAXII resulted overexpressed.

Seminars and congress: ▪10-07-19 "Prolyl hydroxylases: from oxygen sensors to therapeutic targets" prof. Cormac T. Taylor, University of Siena. ▪01-22-20 "Caratteristiche biochimiche e binding partners del SERCA1: verso una migliore comprensione della miopatia di Brody" prof Gaetano Vattemi, University of Siena. ▪04-22-20 Webinar "Run your Western Blott in less than four hours" by ThermoFisher. ▪04-29-20 Webinar "Western blot: Total Protein Normalization (TPN) e tecnologia No-Stain" by ThermoFisher. ▪11-14/17-19 IV carbonic anhydrases satellite meeting. Parma.

Poster and Paper: ▪Poster: "Impairment of human breast and melanoma cancer cell migration by newly synthetized carbonic anhydrases inhibitors". G.G., S.M., A.M., C.A., Y.C., M.M., A.N., F.C.). ▪Article "Hypoxia shapes autophagy in TLR-4 activated dendritic cells." S.M., C.A., D.R., G.G., I.F., C.U., G.M., S.S., F.C., A.N. is currently under revisions.