Phospho-TCTP and Dihydroartemisinin: a Novel Therapeutic Opportunity in Advance Breast Cancer

The Lucibello’s laboratory carries out basic and preclinical research in order to identify novel prognostic markers and therapeutic targets in cancer therapy. In particular, our interests are focused on the activity of Translationally Controlled Tumour Protein (TCTP), a highly conserved protein that plays crucial roles in different physiological processes including cell proliferation and resistance to stress. We have found that high levels of the nuclear phosphorylated form of TCTP (phospho-TCTP) in HER2-positive breast cancer (HER2+ BC) are associated with adverse prognostic factors and with a poor clinical response to trastuzumab therapy (a mAb widely used for HER2-positive) suggesting a possible application of phospho-TCTP as a new marker for breast cancer. Our interest are also focused on the anti-tumor of Dihydroartemisinin (DHA). DHA is the active metabolite of artemisinin, the active principle of Artemisia annua. We have found that DHA, by reducing the expression levels of the phosphorylated form of TCTP, enhances sensitivity to chemotherapy and anti-HER2 antibodies.

In particular, our studies are focused on: i) a proper design and analysis methods for drug combination studies in order to identify synergistic associations among drugs at concentrations achievable in the clinic; ii) the molecular mechanism of inhibition of the most effective synergistic combinations in vivo and in vitro; iii) characterization of phospho-TCTP as a new prognostic factor in the clinical management of patient cohorts with aggressive breast cancer disease.

This study provides the rationale for the design of a new clinical protocol to assess the anticancer activity of the trastuzumab emtansine (T-DM1, an anti-HER2 antibody-drug linked to the anti-mitotic agent emtansine) and DHA combination in patients with HER2-positive breast cancer. This project is led by Lucibello’s laboratory at the IFT-CNR with the involvement of others two partners: IRCCS-Regina Elena National Cancer Institute and Medical Oncology Unit and Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy. This research is supported by Roche S.p.A.

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