Cancer Molecular Analysis by ‘OMIC’ and ‘Cancer Modeling’

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My research program focuses on cancer, by integrating broad disciplines centered on translational sciences. My key research activities include:

- **Molecular Characterization of Melanoma**
  - Using an ‘omic’ approach, aimed at the identification of molecular biomarkers and/or networks associated to its progression which could be exploited for the development of innovative and efficacious therapeutic strategies (1, 2). These studies contributed to the identification of a novel melanoma-associated molecular pathway, where Ran, Aurora Kinase A (AurkA) and TERT were up-regulated while c-myc and PTEN were down-regulated (3). Starting from this observation, my published research demonstrated that AurkA inhibitor plus MEK inhibitor or in triple combination with B-RAF inhibitor might offer a therapeutic alternative for patients without B-RAF mutations or for B-RAF mutated melanomas, respectively (4).

- **Drug Resistance Mechanisms in Cancer**
  - I have highlighted the role of c-myc in drug-response of melanoma to the class of chemotherapeutics, inducing $\text{H}_2\text{O}_2$ accumulation (5) and I have characterized the phenotypic properties of human melanoma cells resistant to dabrafenib, a B-RAF inhibitor drug, used for treatment of patients carrying metastatic melanoma (6). Ongoing studies are aimed at investigating the metabolic properties of these drug-resistant cancer cells with the purpose to use both phenotype and metabolic profiling data to identify new targets for biological drugs development.

- **Cancer Modeling for Personalized Medicine**
  - We need new strategies to better personalize drug therapies, and better approaches to combat drug resistance. Systems biology can be the common platform for classifying disease states, biological networks, and drug response.
  - Breast cancers are comprised of heterogeneous populations of tumors cells characterized by molecular profiles that distinguish each cell subpopulation from one another. During treatment, tumor “subclones”, defined as a set of unique cells within a tumor, follow unique evolutionary and resistance trajectories.
  - In my laboratory, we are developing patient derived breast cancer organoids, which we are characterizing at molecular level (by ‘omic approach’) as well as phenotypically, in order to identify molecular profiles matching disease to biology to drug to effectively treat patients. These studies are critical to identify points of vulnerability for drug targeting. Therefore, by blocking critical resistant phenotypes we can block the transition of tumors to a resistant state.
  - Furthermore, research and development studies are ongoing in order to identify potential anticancer agent candidates for cancer treatment deriving from vegetables (7).

References:


*Phenotype Characterization of Human Melanoma Cells Resistant to Dabrafenib.* Oncology Reports, **2017**, 38: 2741-2751.

7. Mandrich L, **Caputo E**. 

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