Propositions

Accompanying the thesis

"Discovery of Protein Biomarkers Associated to Tamoxifen Resistance"

1. Laser capture microdissection is a robust technique that allows accurate analysis of the tumor proteome (this thesis).

2. The 4-protein signature is the first proteomic classifier of tamoxifen therapy outcome in estrogen receptor positive breast cancer patients developed and validated using proteomic technologies (this thesis).

3. Immuno multiple reaction monitoring (iMRM) mass spectrometry (MS) assays offer a straightforward and robust technology for protein quantitation. Such technique achieves significant prediction of tamoxifen therapy outcome using both tissue and serum specimens (this thesis).

4. Immunohistochemicalanalysis revealed that ANXA1 and CALD1 are independent predictive markers, opening possibilities for alternative targeted therapies(this thesis).

5. Tumors expressing PSAT1 harbor dysregulation of metabolic and immune signaling pathways (this thesis).

6. Targeted therapies in breast cancer generally suppress a single pathway. New strategies will likely target multiple networks in order to minimize the arise of resistance mechanisms (Johnston, J. Natl. Cancer Inst. 2015; 107(10), djv212).

7. The biological mechanisms of cancer, as well as their clinical outcome, do not only rely in the tumor itself but derive from an

interplay between different cellular factors. Tackling these issues will make personalized medicine a reality (Alexander S et al., Curr. Opin. Cell Biol. 2013; 25(5): 659-71; Klement GL, Sci. Transl. Med. 2016; 8(327): 327fs5).

8. Integrated proteogenomic analysis…will enable new advances in cancer biology, diagnostics and therapeutics (Zhang et al., Nature 2014; 513(7518): 382-7).

9. It is essential for clinicians and basic scientists to continue hypothesis-directed pursuit of new biomarkers and targeted therapies, but in order to do so we must better understand each other(Schott et al., Cancer Res. 2015; 75(10): 1930-5).

10. Understanding the subclonal architecture of tumors should finally allow researchers to incorporate the evolutionary perspective into the design of more accurate preclinical models that reflect tumor heterogeneity (Polyak et al., Nat. Med. 2014; 20(4): 344-6; Hiley et al., Cancer Discov. 2016; 6(2): 122-4).

11. Biomarker research has been rapidly advancing in recent times, so fast that fundamental research cannot always keep the pace. Each biomarker study should be designed to include functional experiments in preclinical models(Tommaso De Marchi).