Melanoma multiomics under the magnifying glass of the Regina Elena and San Gallicano Institutes

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Background: Quite unusual in Italy, the twin Regina Elena (IRE) and San Gallicano (ISG) Institutes encompass the whole range of expertise from early dermatological diagnosis, to surgery and medical therapy, involving disciplines as diverse as radiomics, genomics, epigenetics and cellular/molecular biology.

Methods: IRE and ISG have implemented a patchwork of active multidisciplinary groups that glue clinics and research together through the Melanoma 4P (Precision, Personalized, Predictive, Participated) project. It acts as a backbone, providing systematic recruitment/distribution of clinical materials (>700 tissue and liquid biopsies biobanked in 4 years from 258 patients) and associated data, and sets the stage for multi-analyte (RNA, miRNA, DNA, and proteins) monitoring throughout disease course.

Results: With a major focus on understanding pharmacological resistance and develop innovative therapies, our results indicate:
- Inhibiting semaphorin 6A reverts resistance to target therapy;
- In melanoma stem cells, characterized by altered lipid metabolism, SCD1 inhibition restores the response to targeted therapies, e.g.BRAF/MEK inhibitors;
- OncomiRNA/oncosuppressor miRNAs ratio predicts response to target therapies and is the subject of novel predictive metrics and patents;
- Higher level of Semaphorin 5A and 7A transcript has been detected in patients with advanced melanoma;
- Bcl-2 family protein expression affects therapy response.

Moreover:
- Original approaches of Computerized Tomography (CT) Texture Analysis are being implemented to extract quantitative imaging features, particularly relevant to understanding tumor microenvironment and response to immune checkpoint blockade;
- Organoids are being established in the context of an Alliance Against Cancer collaborative network;
- As to advanced molecular diagnosis, special emphasis has been given to nanophotonic liquid biopsy (Versilib EU project) and actionable molecular alterations not yet approved by regulatory bodies (e.g. OncoKB level 3A/B) in collaboration with our institutional Molecular Tumor Board (MTB).
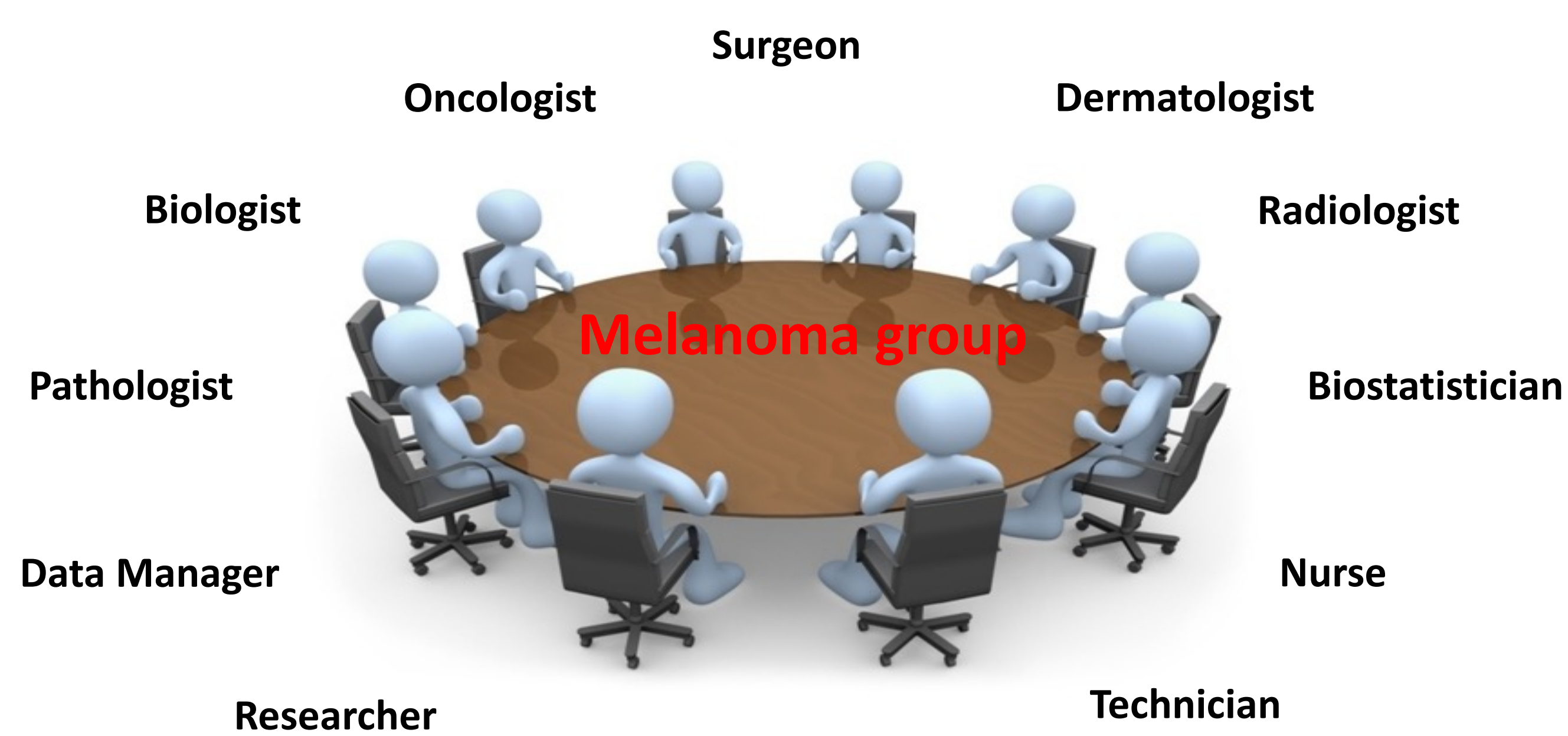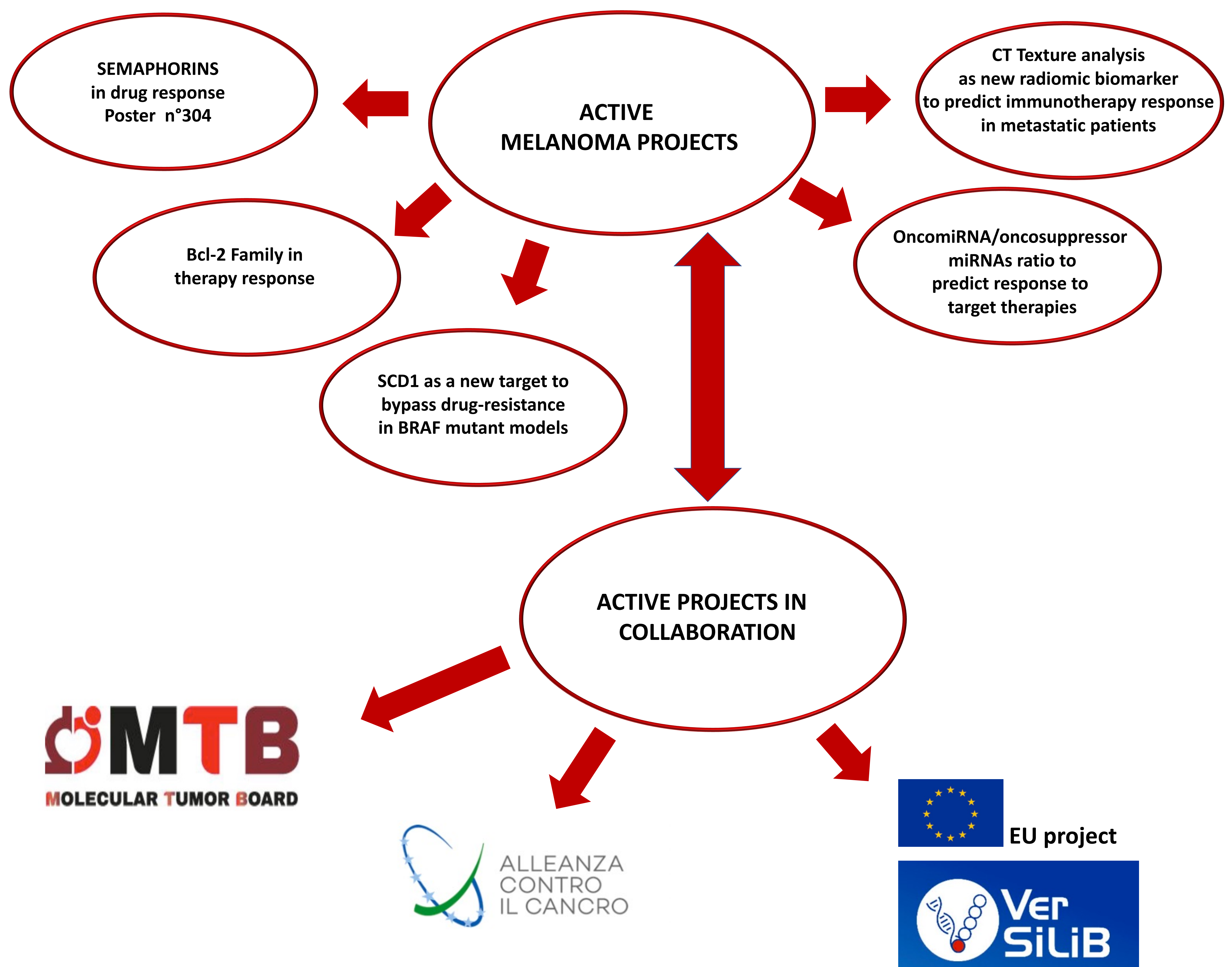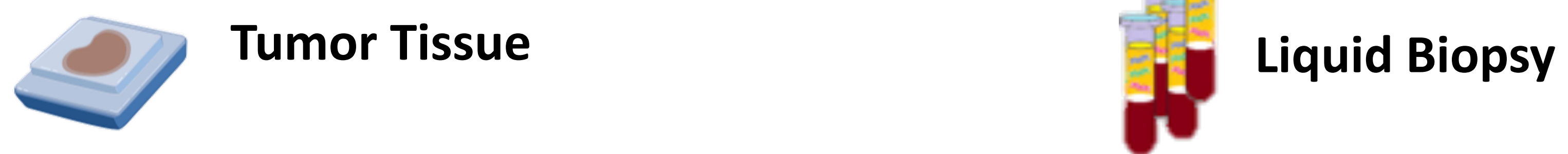
Conclusions

IRE and ISG outline a novel comprehensive strategy for comprehensive melanoma management and understanding.