Spatial Proteomic Profile (SPP) of Epithelioid Sarcoma

Epithelioid sarcoma (ES) is a rare soft tissue sarcoma (incidence ~0.02–0.05/100,000) affecting young adults.[1] It is an aggressive tumor and generally presents as a painless, slow-growing mass in the distal extremity of young adult. Unlike other sarcomas, ES frequently metastasizes to regional lymph nodes and distant sites, commonly to the lungs.[2] Complete surgical resection is curative for primary, localized tumor; while for advanced stage recurrence often occurs. [3]

Depending on the anatomical localization of the tumor, ES is classified into two subtypes: a classic form (C-ES) that occurs on the extremities as a slow-growing nodule, and a proximal (P-ES) form that occurs in deeper areas of the pelvis, perineum, and genital tract.[4] P-ES is usually more aggressive than C-ES, for the higher rate of recurrences and earlier development of metastases.[5]

ES cells show epithelioid morphology with co-expression of mesenchymal and epithelial markers.[2]

Until now, the only recurrent genetic alteration described in ES is the functional inactivation of SMARCB1 (SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1), a key component of the SWI/SNF chromatin remodeling complexes. Loss of SMARCB1/INI1 protein expression was observed in approximately 90% of classic and proximal ES cases.[6] How SMARCB1 deficiency induces the clinicopathological characteristics of ES and which other molecular events concur to its malignancy is still under investigation.

To gain insights into the molecular basis of the malignant features of ES, a global molecular analysis would therefore be effective. The present project will adopt global proteomics approaches to investigate primary tumor tissues of ES. In particular, we will identify proteins showing differential expression between tumor tissues and surrounding non-tumor tissues obtained from ES patients. Moreover, the project will differentiate the analysis of proteins residing on the cell membrane, which could serve as biomarkers or molecular targets[7], from the cytosolic proteins, revealing specific molecular signatures. This study will include ES tissues obtained from the Istituto Ortopedico Rizzoli biobank.

Proteins that will be differently expressed will be monitored in ES established cell lines differing in their invasive potential and aggressiveness, in order to further understand the biology behind ES protein signature. The data obtained from this study will be useful for finding novel biomarkers and developing new therapies.

References:

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Timeline and cost:

For this pilot study, aiming at identifying novel ES biomarkers/targets, the following milestones are envisioned:

- Identification of proteins differentially expressed on ES tissues cell surface (months 0-8)

- Validation of the identified markers in ES cell lines (months 6-12)

Cost: 8000-10000 euro (depending on the number of analyzed samples)

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