P-189

MALIGNANT PLEURAL MESOTHELIOMA ORGANOIDS AND PATIENT DERIVED XENOGRAFTS (PDX): NEW FRONTIERS OF IN VIVO AND IN VITRO MODELS TO STUDY DRUG SENSITIVITY AND TUMOR ENVIRONMENT

Margherita Cattaneo[1], I. Righi[1], P. Mendogni[1], A. Cherubini[3], F. Salanitro[2], R. Piras[2], L. Lazzari[2], R. Affatato[4], F. Ricci[4], M. Marabese[3], M. Nosotti[1], L. Rosso[1]

[1]*Thoracic Surgery and Lung Transplantation Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*

[2]*Dipartimento di Medicina Trasfusionale ed Ematologia, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy*

[3]*Laboratory of Molecular Pharmacology, IRCCS Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy*

Objectives:

Malignant pleural mesothelioma (MPM) is a rare and aggressive cancer with poor prognosis. A therapeutic gold-standard does not exist, so the treatment is still object of investigations. Clinicians and researchers need to improve efforts in precision medicine oncology using new model systems. Since the inflammatory and immunological MPM context is crucial, organoids and Patient-Derived Xenografts (PDX) can be a model for a better knowledge of tumor microenvironment and for testing the efficacy of new therapeutic options. The final goal is to use them as a tool to predict response to anti-cancer drugs in individual patients.

Methods:

For PDX, tumor specimens were fragmented and implanted in the flank of immunodeficient mice. Tumors grown in mice were aseptically removed and re-implanted in other animals to obtain a second generation. Tumor fragments were fixed in formaldehyde for pathological examination. Human pleural and MPM biopsies were processed to obtain organoids. Briefly, pleural tissues were digested using Collagenase and successively embedded in matrigel with specific basal medium. After 21 days, the size and shape of organoids were measured, and gene expression analysis of specific pleural organoid markers was performed. The samples were collected after informed consent and Ethical approval.

Results:

PDXs were successfully obtained. The pathological characterization showed that models recapitulate the human tumors they originate from. Organoids were obtained and expanded till the third passage. By qPCR, an increased of specific organoid markers was observed.

Conclusions:

We successfully generate PDXs with the same gene expressions of the native MPM. We also demonstrated that organoids can be obtained from non tumoral pleura and MPM recapitulating the organoid features. These MPM PDX-organoid platforms can provide a variety of important biological parameters of the disease for drug testing, high throughput screens, and disease modelling and can be important to better understand the pathogenesis and the treatment options.

Disclosure: No significant relationships.
Keywords: patient derived xenograft, organoid, malignant pleural mesothelioma