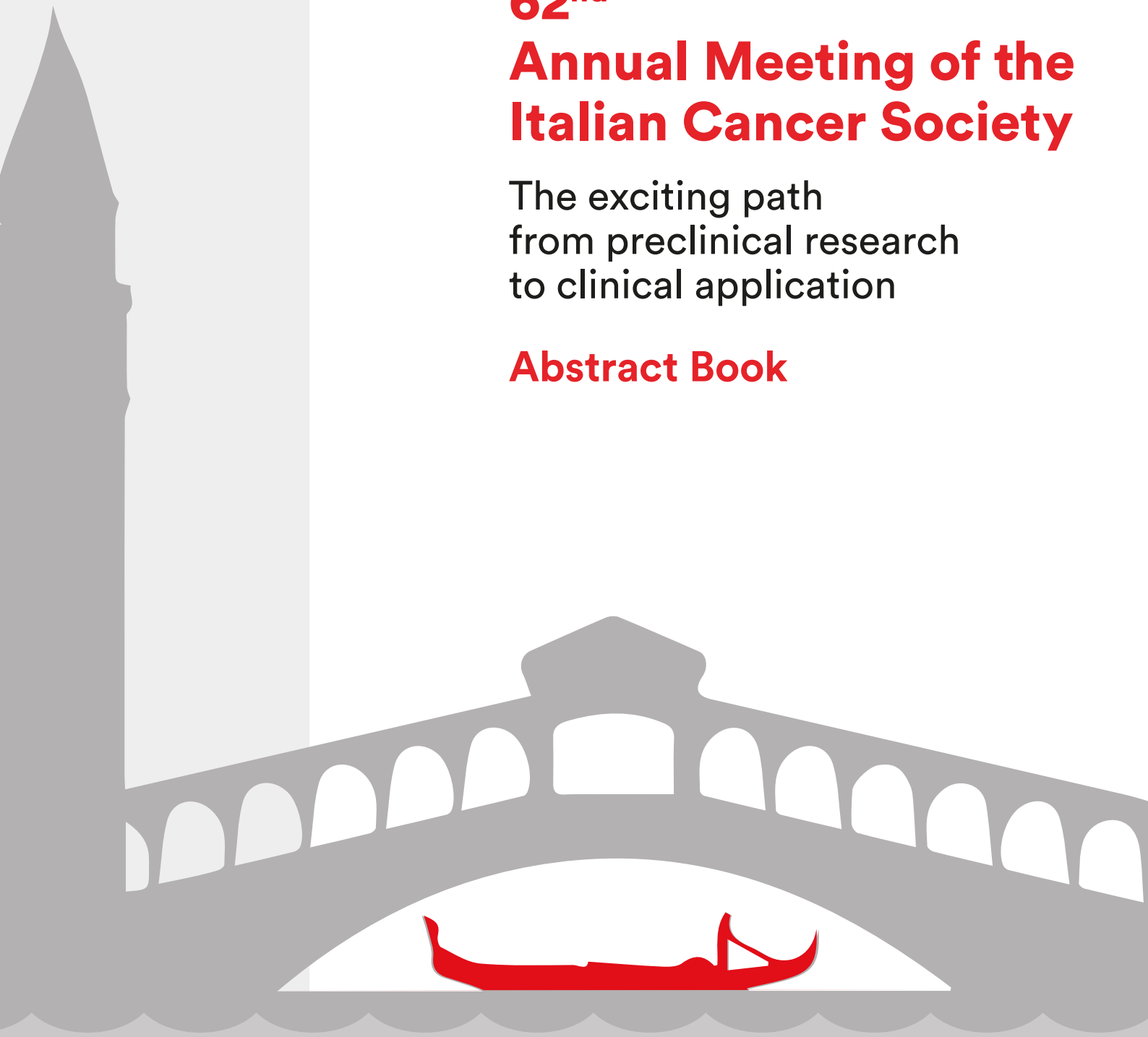
SIC

62nd Annual Meeting of the Italian Cancer Society

The exciting path
from preclinical research
to clinical application

Abstract Book



Venice, November 16-18, 2022

62nd Annual Meeting of the Italian Cancer Society

The exciting path
from preclinical research
to clinical application

Venice
November 16-18, 2022

Scientific Coordinators

Gustavo Baldassarre
Head of the Molecular Oncology Unit,
Centro di Riferimento Oncologico di Aviano (CRO), IRCCS National Cancer Institute (NCI), Aviano (PN), Italy

Fabio Puglisi
Head of the Department of Medical Oncology,
Centro di Riferimento Oncologico di Aviano (CRO), IRCCS National Cancer Institute (NCI), Aviano (PN), Italy
Professor of Medical Oncology,
Head of the School of Medical Oncology,
Department of Medicine,
University of Udine, Italy.

Local Scientific and Organizing Committee

Barbara Belletti
IRCCS, Centro di Riferimento Oncologico di Aviano, Aviano (PN), Italy

Vincenzo Canzonieri
IRCCS, Centro di Riferimento Oncologico di Aviano, Aviano (PN) University of Trieste Trieste (TS), Italy

Saverio Cinieri
"Sen. Antonio Perrino Hospital", Brindisi - AIOM President Brindisi (BR), Italy

Pierfranco Conte
Istituto Oncologico Veneto IOV-IRCCS, University of Padova Padua (PD), Italy

Giannino Del Sal
University of Trieste - Trieste (TS), Italy
ICGEB-International Centre for Genetic Engineering and Biotechnology, Trieste (TS), Italy
Trieste IFOM ETS, The AIRC Institute of Molecular Oncology, Milan (MI), Italy

Silvia Franceschi
IRCCS, Centro di Riferimento Oncologico di Aviano, Aviano (PN), Italy

Valter Gattei
IRCCS, Centro di Riferimento Oncologico di Aviano, Aviano (PN), Italy

Valentina Guarneri
Istituto Oncologico Veneto IOV-IRCCS, University of Padova Padua (PD), Italy

Stefano Indraccolo
Istituto Oncologico Veneto IOV-IRCCS, University of Padova Padua (PD), Italy

Roberta Maestro
IRCCS, Centro di Riferimento Oncologico di Aviano, Aviano (PN), Italy

Michele Milella
University of Verona Verona (VR), Italy

Paolo Morandi
"Dell'Angelo" Hospital, Mestre (VE), Italy

Flavio Rizzolio
University Ca' Foscari, Venice (VE), Italy

Aldo Scarpa
University of Verona Verona (VR), Italy

Agostino Steffan
IRCCS, Centro di Riferimento Oncologico di Aviano, Aviano (PN), Italy

Gianluca Tell
University of Udine Udine (UD), Italy

SIC Scientific Board

PRESIDENT
Nicola Normanno
National Cancer Institute, G. Pascale, Napoli Naples (NA), Italy

PRESIDENT ELECT
Maurizio D'Incalci
Humanitas Research Hospital and Humanitas University, Milan (MI), Italy

PAST PRESIDENT
Gabriella Sozzi
Fondazione IRCCS National Cancer Institute, Milan (MI), Italy

BOARD
Paola Allavena
Humanitas Research Hospital, Milan (MI), Italy

Gustavo Baldassarre
IRCCS, Centro di Riferimento Oncologico di Aviano, Aviano (PN), Italy

Fabrizio Bianchi
IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy

Giovanni Blandino
Regina Elena National Cancer Institute, Rome (RM), Italy

Antonino Bruno
University of Insubria, Varese (VA), Italy and IRCCS MultiMedica, Milan (MI), Italy

Paola Chiarugi
University of Florence, Florence (FI), Italy

Federica Di Nicolantonio
University of Turin and Candiolo Cancer Institute FPO-IRCCS Turin (TO), Italy

MEMBERS UNDER 35
Ilaria Guerriero
Biogem, Institute of Biology and Molecular Genetics, Ariano Irpino (AV), Italy

Erica Torchiaro
Candiolo Cancer Institute FPO-IRCCS, Torino Turin (TO), Italy

Contents

H9

Epigenetic investigation onto circulating microRNA 197-3p reveals its different dysregulation in sera from malignant pleural mesothelioma affected patients and workers ex-exposed to asbestos fibers

Di Mauro G. [1], Frontini F. [1], Torreggiani E. [1], Iaquinta M.R. [1], Mazziotta C. [1], Mazzoni E. [2], Martini F. [1], Bononi I. [3], Tognon M. [1]
(1) Department of Medical Sciences, Laboratories of Cell Biology and Molecular Genetics, School of Medicine, University of Ferrara, Ferrara - Italy, (2) Department of Chemical, Pharmaceutical and Agricultural Sciences-DOCPAS, University of Ferrara, Ferrara - Italy, (3) Department of Translational Medicine, University of Ferrara, Ferrara - Italy

In recent years, the epigenetic role of microRNAs (miRs) in many different human cancers has been reported. It turned out that microRNAs behave as activated oncogenes or tumor suppressor genes. Identifying dysregulated miRs in tumors, alongside their target genes, seems to be a promising approach for innovative anti-cancer therapies, especially in those tumors, which are still fatal such as malignant pleural mesothelioma (MPM). In this study, an epigenetic investigation was carried out onto circulating miR-197-3p, which has been found to be associated to human tumors of different histotype. To this purpose, serum samples from patients affected by malignant pleural mesothelioma (MPM; n=60), workers ex-exposed to asbestos (n=60) and healthy subjects (HS; n=60) were comparatively studied. MiR 197-3p expression level was quantified using Real-Time qPCR and the more analytical droplet digital PCR. Clinicopathological characteristics, occupational, non-occupational information and overall survival (OS) were evaluated in correlation studies. In the MPM cohort, a mean of 507.2 and 880.2 copies/µl of miR-197-3p cDNA were detected by RT-qPCR and ddPCR, respectively. Levels of miR-197-3p were significantly lower in the MPM cohort compared to HS with both PCR methods, p=0.0159* and p=0.0381*, respectively. OS data were significantly associated with histological subtype and pleurectomy. In WEA sera miR-197-3p level was significantly lower than HS, with 2.6-fold down-expression (p = 0.0001***). Whereas, the miR-197-3p quantity tested slightly higher, by RT-qPCR and ddPCR, in the MPM than in the WEA cohort (mean of 336.0 copies/µl of miR-197-3p and mean of 525.0 copies/µl, respectively). In addition, an inverse correlation was found between the expression of miR-197-3p and the cumulative asbestos exposure in WEA sera. Based on our data and considering the involvement of miR-197-3p target genes in the regulation of the inflammatory response, we may speculate that this miR could promote an unbalanced inflammatory process, resulting from exposure to asbestos fibers. Ongoing functional studies will clarify the role of miR-197-3p in MPM. In conclusion, circulating miR-197-3p is proposed as a new potential biomarker of the MPM onset and asbestos exposure in WEA.

H10

New target molecules make T regulatory cells unique in Malignant Mesothelioma

Oliveto S. [1,5], Ritter P. [1,4], Miluzio A. [1], Gruarin P. [1], Curti S. [1], Benvenuti M.R. [2], Novellis P. [3], Veronesi G. [3], Raimondi M.T. [4], Abrignani S. [1] and Biffo S. [1,5]
(1) INGM, National Institute of Molecular Genetics "Romeo edEnricaInvernizzi", Milano, Italy, (2) Thoracic Surgery Unit, Spedali Civili of Brescia, Brescia, Italy, (3) Division of Thoracic Surgery, San Raffaele Scientific Institute, Milan, Italy, (4) Politecnico of Milan, Milan, Italy, (5) DBS, University of Milan, Milan, Italy

Blockade of immune checkpoints, such as inhibition of CTLA-4 and PD-L1 is the master approach to boost antitumor immunity. Unfortunately, long-lasting responses miss in most patients, due to the persistence of immunosuppressive mechanisms. T regulatory cells constitute a T cell subset that controls the activity of effector T cells and are fundamental for the maintenance of immune tolerance. They have a highly immunosuppressive ability and support the tumor in escaping the immune defence. We characterized the immune microenvironment and particularly tumor infiltrates of several Malignant Mesotheliomas. CD4+ FOXP3+ cells are spread in the MPM tissues and Foxp3+ cells are specifically organized in the infiltrates' periphery and have high immunosuppressive capabilities. We isolated intratumoral CD4+ Treg from surgical chemonaive MPM samples and characterized their molecular signature. They upregulated several immune checkpoint genes and a specific set of cytokines and citokine receptors. Surprisingly, they expressed also a set of genes never described before underlining the uniqueness of the immunosuppression in MPM. Because targeting specific Treg cells by manipulating tumor-derived signals may become a novel approach for MPM treatment, we developed a microfluidic based analysis for studying tumor-TILs interaction. TILs can be circulated on a 3D scaffold where some adhere and can be rescued for the analysis of the immunoediting control.
Methods: 1. MPM samples are plated in a special matrix and cells cultures are estabilished. 2. We microengineered a 3D scaffold that hosts tumoral cells derived from MPM biopsies via a two-photon laser polymerization (2PP) technique. 3. Chemonaive MPM samples are collected (n=10) and infiltrating CD4+ Tregs are subjected to bulk RNA-sequencing and CITE-Seq analysis, in comparison to matched blood Tregs and NSCLC infiltrating Treg cells. 4. We characterized Tregs molecular signature and immune microenvironment.
Results: We obtained high efficiency in maintaining primary MPM cells, which retrieve native tumors. Primary lymphocytes are circulated by a microfluidics pump on the tumor scaffold where they are maintained alive and some are able to adhere. We show that MPM are highly infiltrated with CD4+ Tregs which are spread in the tissues. Foxp3+ cells are specifically organized in the infiltrates' periphery and have high immunosuppressive capabilities. Transcriptional analysis shows that Tregs upregulate several immunosuppressive genes and a specific set of cytokines and citokine receptors. Surprisingly, they expressed also a set of genes never described, underlining the uniqueness of the immunosuppression in MPM.
Conclusion: Immunesuppression is part of the developmental program of MPM tumor cells. Manipulation of tumor-derived signals targeting specific Treg cells may ameliorate MPM therapies and treatment.