

## **Narrative sketch**

Claudio Tripodo is Full Professor of Pathology at the University of Palermo, Director of the Tumor Immunology Research Unit of Department of Health Sciences in University of Palermo, and from 2019 head of Histopathology and Tumor Microenvironment Program in IFOM (Institute FIRC of Molecular Oncology) in Milan. He is a very talented researcher with specific expertise in the field of diagnostic and experimental pathology of cancer.

Among the received prestigious awards, the most important is “Giuseppe Della Porta” Award 2019 of AIRC Foundation. Since June 2016 he is member of the scientific committee of the Italian Association for Cancer Research (AIRC).

He is author of 223 publications in international peer-reviewed journals from 2004, with a H-index of 49 with 8269 citations (Scopus Database). He is member of the Editorial Board of Cancer Research of the American Association for Cancer Research and member of the European Bone Marrow Working Group (EBMWG) of the European Association of Hematopathology (EAHP). He has attended as invited speaker at several international conferences.

The fil rouge of his research activity has been centered on the study of the tumor-associated immunological and stromal microenvironment with particular attention to the role of extracellular matrix constituents in the regulation of inflammatory processes sustaining the neoplastic clone arousal and their activity on the establishment of a permissive microenvironment for cancer progression. Claudio Tripodo was currently investigating the reciprocal influence of immune cells and stromal elements of the tumor microenvironment on the development and progression of solid and haematological cancers. In fact, stromal constituents may have anticancer activities by regulating immunosuppression and restraining carcinogenesis. He has examined the tumor microenvironment, recognizing it as a key factor in multiple stages of disease progression and a pathological active niche that shapes tumor evolution.

During his research activity, Tripodo gained documented experience in the field of haematopathology and pathology of the immune system and specifically in lymphoproliferative and myeloproliferative neoplasms and related disorders. Moreover, he has contributed to research advance in dissecting the components of tumoral microenvironment and highlighting its potential in order to identify new tools for recognition of early stage of disease and new biological targets. His researches suggest that conventional therapies should be combined with microenvironment-targeting treatments to achieve optimal clinical outcomes. Overall, these progressing aspects of microenvironment studies provide a significant guideline for prospective development of personalized medicine, with the long term aim of providing a cure for specific cancer.

During his visiting in Trieste, he gained knowledge about immunology with Prof. Tedesco and started to evaluate the potential role of complement system in solid and hematopoietic malignances. Fast growing cancer cells develop strategies to escape immune defences. They can trigger local inflammation that in turn promotes disease progression rather than controlling tumor growth. This process is characterized by the peri-tumoral recruitment of leucocytes with immunosuppressive properties such as tumor associated macrophages, myeloid-derived suppressor cells (MDSCs) and regulatory T cells. Complement is one of the immune players present in the tumor microenvironment as suggested by the findings of

Complement deposits in tumor tissue from patients with various solid tumors. C1q can act as tumor-promoting factor by favouring adhesion, migration and proliferation of cancer cells as well as angiogenesis and metastasis.

From many years Tripodo also dissected the microenvironment in Lymphomas where the pathogenesis is related to a deregulated immunologic stimulation. In this setting he has investigated the effect of stroma-intrinsic features on Splenic Marginal Zone Lymphoma (SMZL) disease progression by focusing on the microenvironment of the bone marrow (BM), which represents an elective disease localization endorsing diagnostic and prognostic relevance. In particular, he has demonstrated the unfavorable prognostic influence of dense CD40 expression by BM stromal cells (BMSC), which involves the contribution of CD40L-expressing bystander mast cells (MC) infiltrating SMZL BM aggregates. The CD40/CD40L-assisted cross-talk between BMSC and MC populating in SMZL microenvironment contribute to the engendering of pro-inflammatory conditions eventually fostering B-cell clone fitness. In the process of reshaping the stromal microenvironment of infiltrated organs/tissues, B-cell clones can be supported by accessory cells of the immune system such as macrophages and mast cells that may be recruited directly by neoplastic cells through the synthesis of cytokines and chemokines. Macrophages and mast cells variably populate the infiltrates of B-cell malignancies molding different aspects of tumor microenvironment, such as angiogenesis and stromal cell proliferation, extracellular matrix remodelling, induction of adhesion molecule expression. Infiltrating accessory cells and stromal cells, through the synthesis of IL-1b, IL-6, and IL-23 cytokines, may contribute to engender a pro-inflammatory environment prone to Th17 generation, inflammatory cell infiltration, and autoimmunity.

During his visiting in IRCCS in Milan, the main focus of his research activity was the biological significance of the matricellular protein SPARC. Despite of the pleiotropic role of SPARC in tissue remodeling is, he investigated whether its expression could have any functional role in the stromal alterations associated with neoplasia, in particular with myeloid malignancies. In this cancer, the neoplastic clone outgrows normal hematopoietic cells leading to bone marrow (BM) failure. This event is also sustained by detrimental stromal alterations, such as BM fibrosis and osteosclerosis, whose occurrence is the harbinger of a dismal prognosis. The matricellular protein SPARC contributes to the stromal remodeling associated with myeloproliferation. The degree of SPARC expression in BM stromal elements correlates with the degree of stromal changes and the severity of BM failure. SPARC deficiency in the radioresistant BM stroma compartment impairs the development of myelofibrosis but at the same time it is associated with an enhanced reactive myelopoietic response to thrombopoietin.

He was involved as group leader and principal investigator in many research grants.

Besides to “Giuseppe Della Porta” Award, he is the winner of the Young Investigator Award of the “Guido Berlucchi” Foundation Borgonato di Corte Franca, Brescia, Italy (15<sup>th</sup> September 2014), “Carlo Chianello” Foundation for Oncological Research, Palermo, Italy (13<sup>th</sup> July 2012) and the “Young Investigator Award” of the “Mediterranean School of Oncology”, Rome, Italy (28<sup>th</sup> January 2011).

From 2004, Claudio Tripodo participated to many national and international meetings as invited speaker and as chairman. He is member of the following societies the Pathology board of the Italian Foundation for the study of Lymphomas (FIL), the Società Italiana di Immunologia Clinica ed Allergologia (SIICA), the Società Italiana di Anatomia Patologica e Citopatologia (SIAPEC) within

it he is the coordinator of Sperimental Pathology Group and lastly co-founder of the Gruppo di Studio della Biologia del Linfoma di Hodgkin (SIES/FIL).