TITLE
Tumor-Associated Macrophages (TAMs)

Overview of the course
When recruited into the tumor microenvironment, circulating monocytes are converted into tumor-associated macrophages (TAMs). Schematically, macrophages grow into two main groups called classically activated macrophages (M1) and alternatively activated macrophages (M2). M2s help tumor cells escape from being killed and help their spread to other tissues and organs. TAMs are recruited by various tumor-derived signals, including, as described by very recent paper, mediators released by tumor cells under programmed cell death (PCD). This course illustrates TAM, promotion of their development in the tumor microenvironment, the role of STAT, key transcription factors mediating macrophage M1/M2 polarization, as well as flow cytometry as a valuable tool for studying TAM in the tumor microenvironment and peripheral blood.

References
Zhou J, Tang Z, Gao S, Li C, Feng Y, Zhou X. Tumor-Associated Macrophages: Recent Insights and Therapies. Front Oncol. 2020; doi: 10.3389/fonc.2020.00188.

Liu T, Zhu C, Chen X, et al. Ferroptosis, as the most enriched programmed cell death process in glioma, induces immunosuppression and immunotherapy resistance. Neuro Oncol. 2022. doi: 10.1093/neuonc/noac033.

Sica A, Mantovani A. Macrophage plasticity and polarization: in vivo veritas. *J Clin Invest*. 2012; doi:10.1172/JCI59643.

Wu K, Lin K, Li X, et al. Redefining Tumor-Associated Macrophage Subpopulations and Functions in the Tumor Microenvironment. *Front Immunol*. 2020; doi:10.3389/fimmu.2020.01731

Schedule (~6 hours)
The course will include three lessons (2 hours each), as it follows.

Programme
Lesson one (Dr. Maria Fiammetta Romano, DMMBM): May 23, Monday, 3:00 p.m.
Seminar room 4th floor Torre Biologica
Cell death, tumor-associated macrophages and immunotherapy resistance

Recent evidence highlights that self-destruction of tumor cells feeds the immunosuppressive microenvironment by promoting alternative macrophage polarization. In turn, generation of tumor-friendly macrophages contrasts checkpoint-targeted immunotherapy.

Lesson two (Dr. Yichuan Xiao, University of Chinese Academy of Sciences, Shanghai): May 24, Tuesday, 10:00 a.m.
Via Zoom
STAT6 acetylation potentiates anti-tumor immunity through inhibition of M2 macrophages

Stat6 is a major player in the alternative M2 macrophage polarization. Recent studies have highlighted that the acetylation of the transcriptional factor by the acetyltransferase CREB-

binding protein (CBP) suppresses M2 activation. CBP is ubiquitinated by Trim24, thus facilitating CBP recruitment to Stat6. Loss of Trim24 inhibits Stat6 acetylation and promotes M2 polarization, thus compromising the antitumor immune responses.

Lesson three (Dr. Simona Romano, DMMBM): May 25, Wednesday, 3:00 p.m.
Seminar room 4th floor Torre Biologica
Strategies and methodology to study subpopulations and functions of TAMs

The controllable activation of macrophages towards desirable phenotypes in vivo and in vitro provides powerful information for in-depth knowledge of TAMs and their crosstalk with other immune cells and malignant tumor cells. Herein an overview on the state-of-art approaches used for TAMs immunophenotyping, identification, and study with a particular focus on traditional and innovative flow cytometric technology.