3rd Cuneo City Immunotherapy Conference (CCITC)

Immunotherapy in hematological malignancies

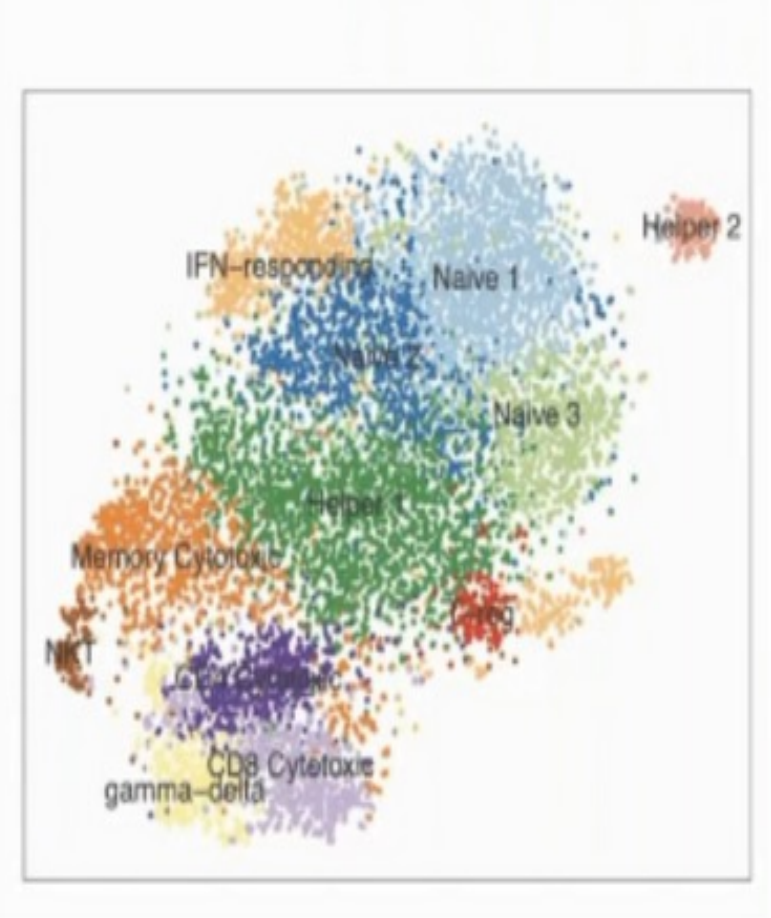
May 18-19-20, 2023

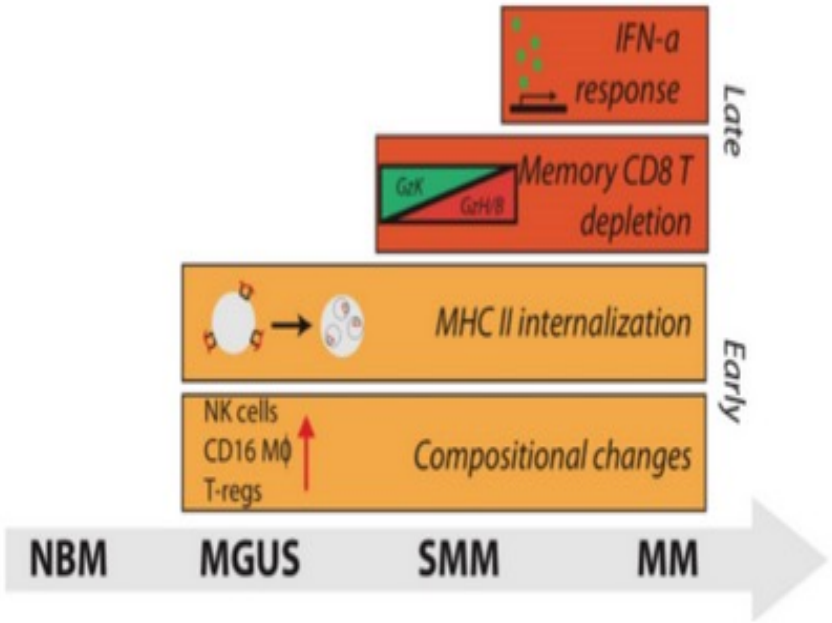
Introduction to lecture prof. Angelo Vacca

by Francesco Di Raimondo,

Catania, Italy

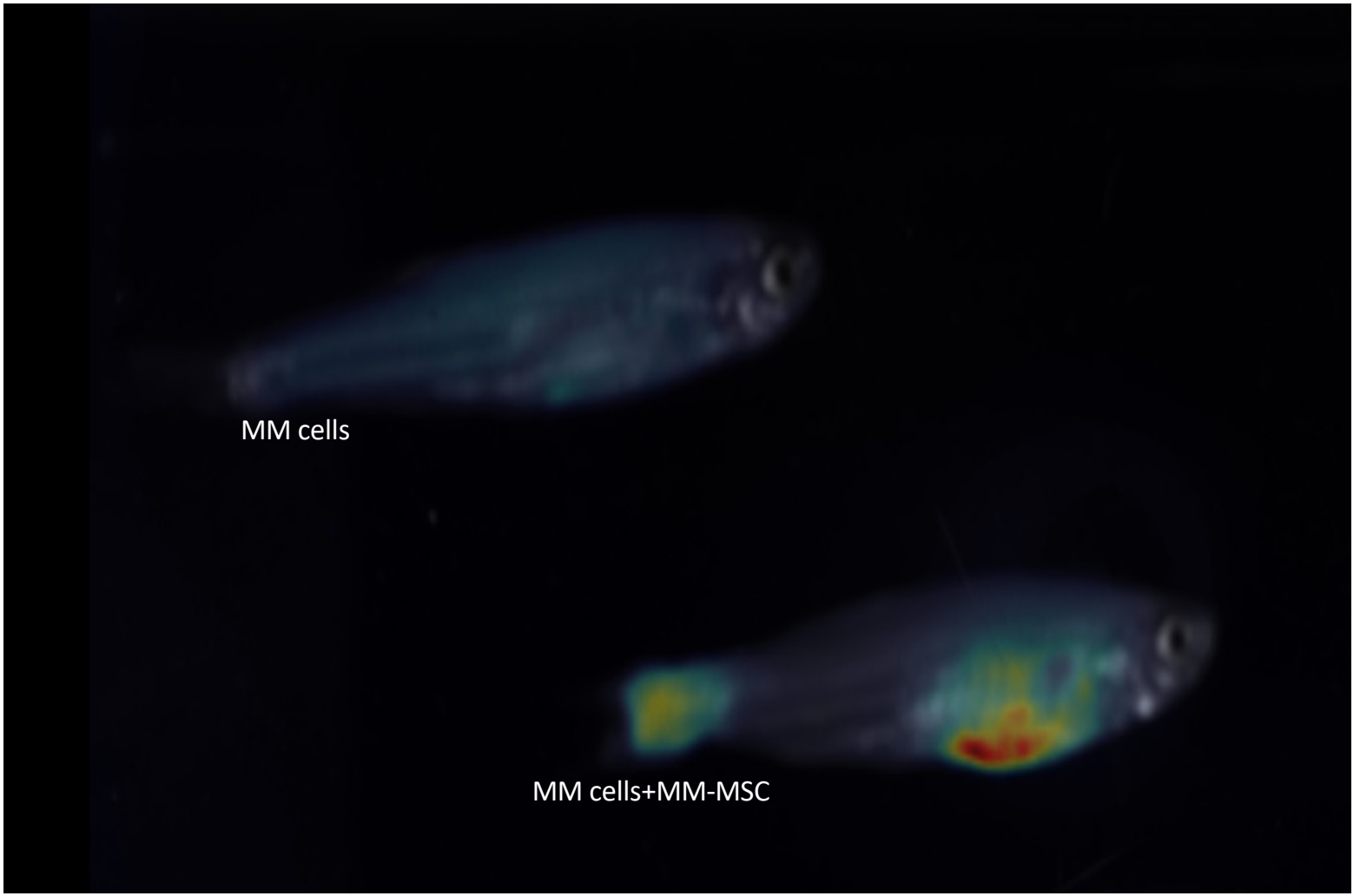
Complex changes in microenvironment composition occurring in Multiple Myeloma evolution



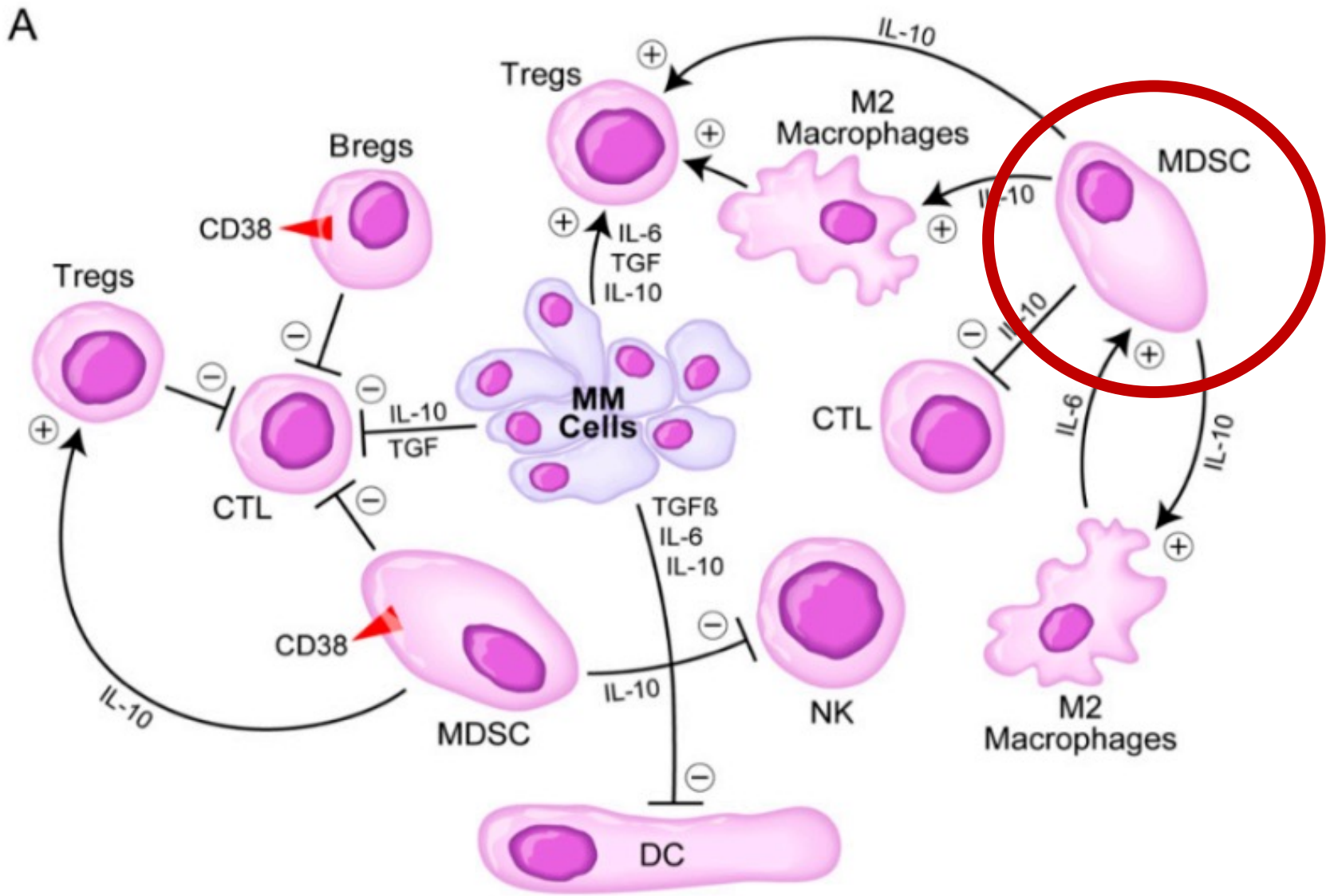


O. Zavidij, Nature Cancer, 2020

Microenvironment

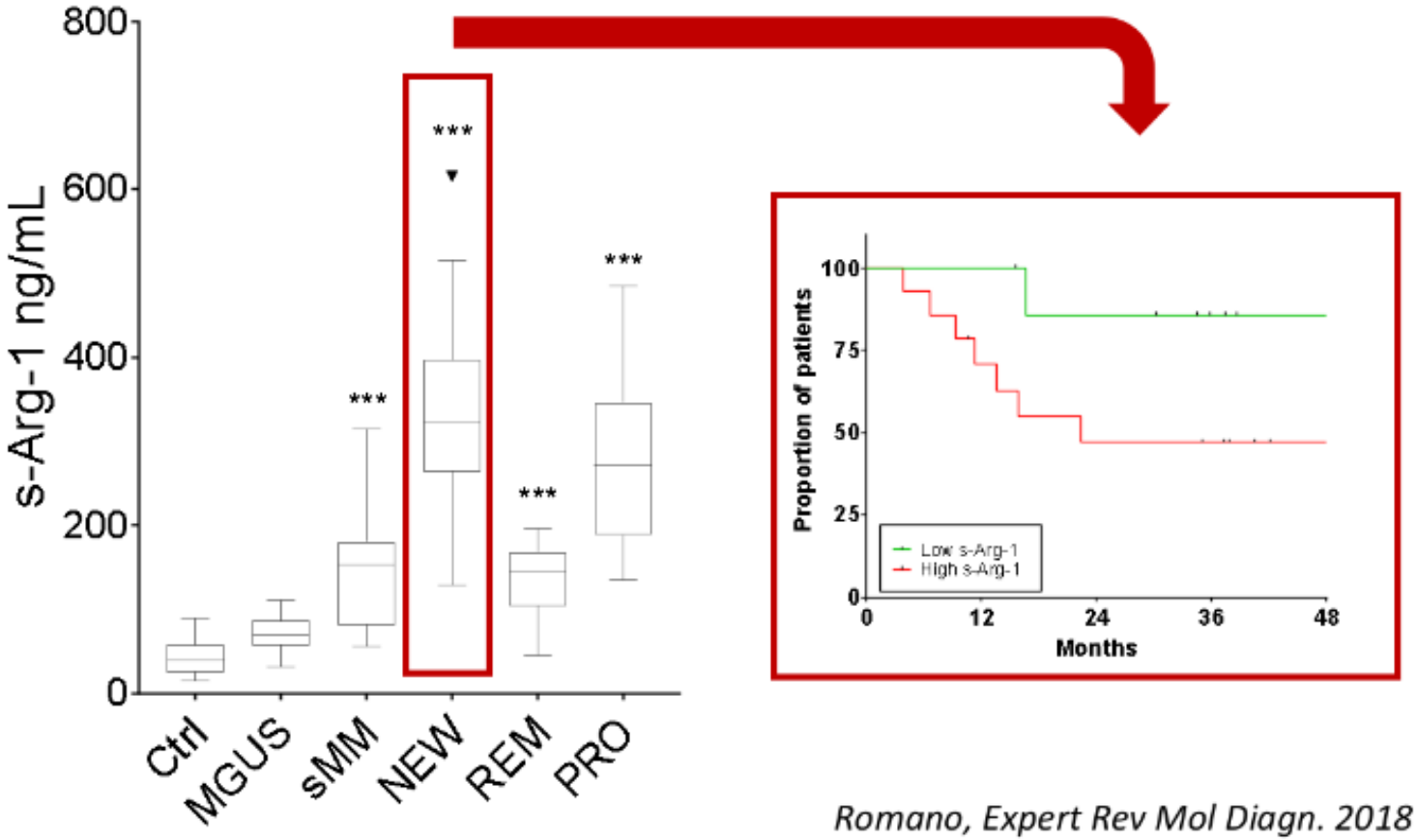


MM-MSC supports MM growth in immunocompetent zebrafish.



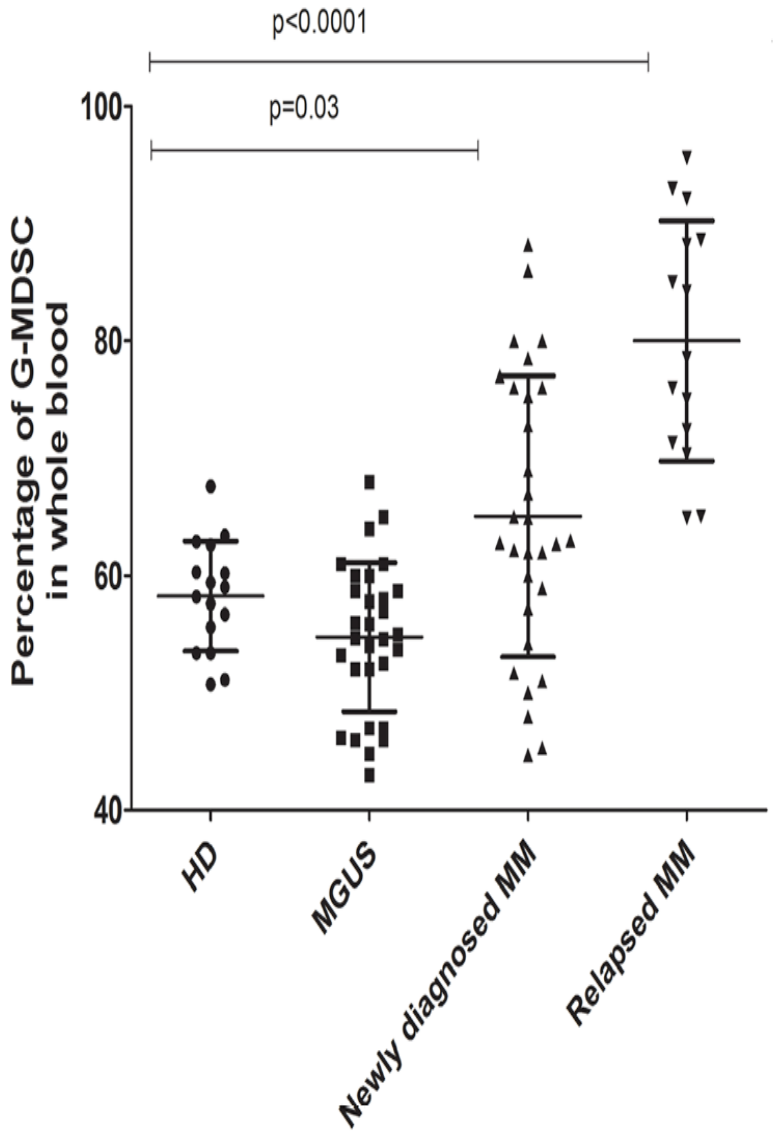
Uckun FM, Cancers 2021

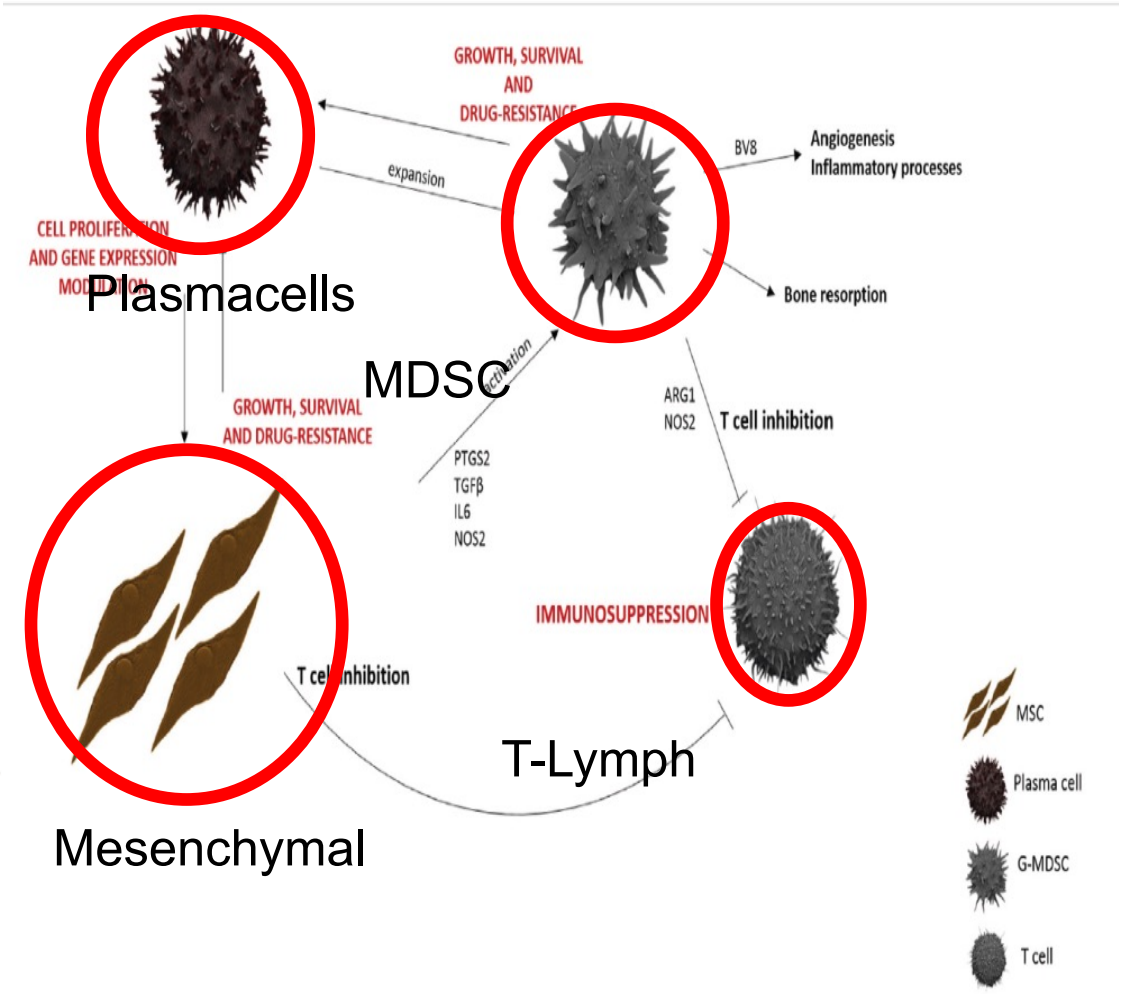
Arginase-1 is increased in high-density neutrophils in Multiple Myeloma and associated to inferior outcome



Romano, Expert Rev Mol Diagn. 2018 Jul;18(7)

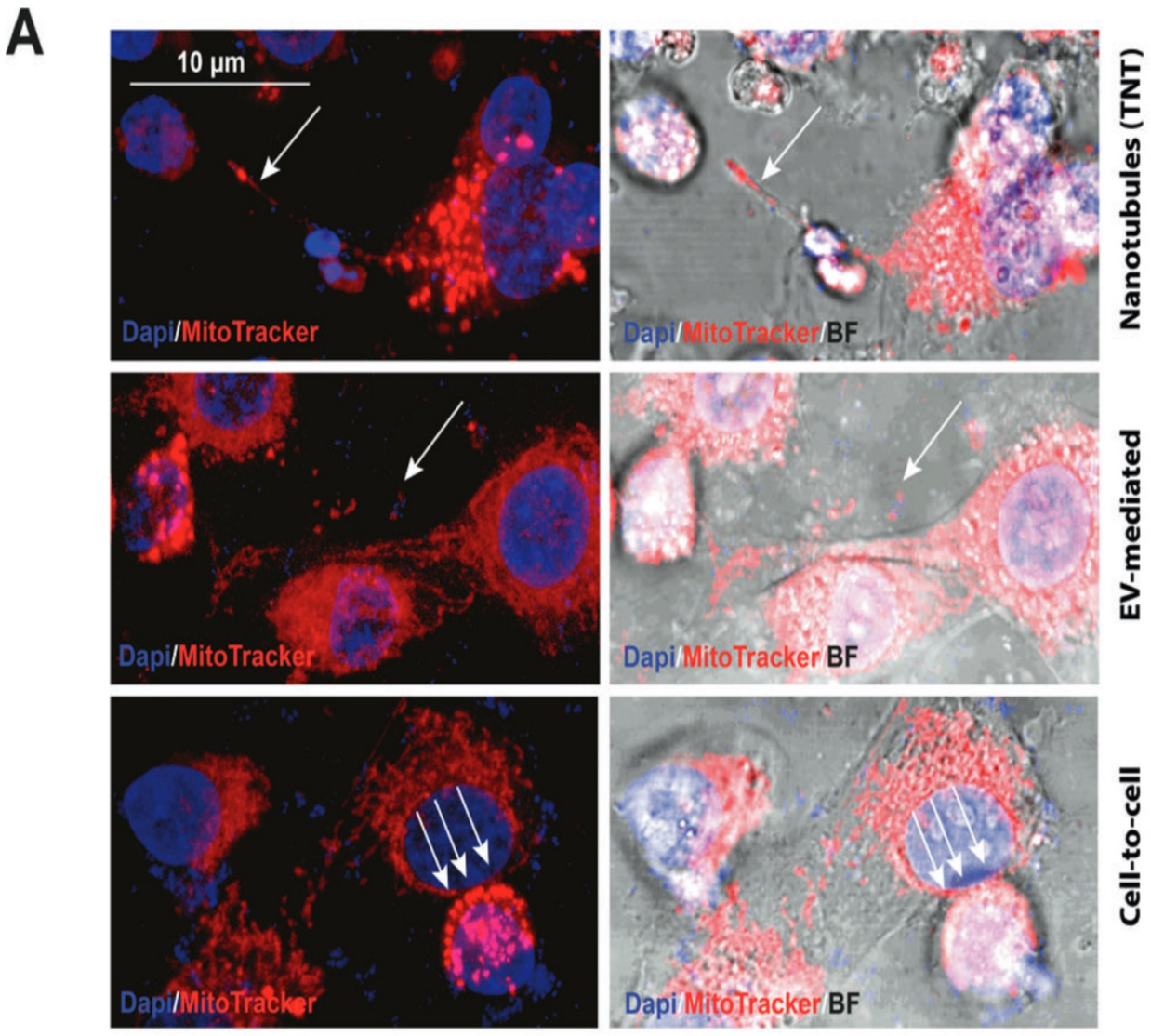
MM-MSC, both directly and through G-MDSC activation, support MM growth, survival and drug-resistance within an immunosuppressive BM microenvironment

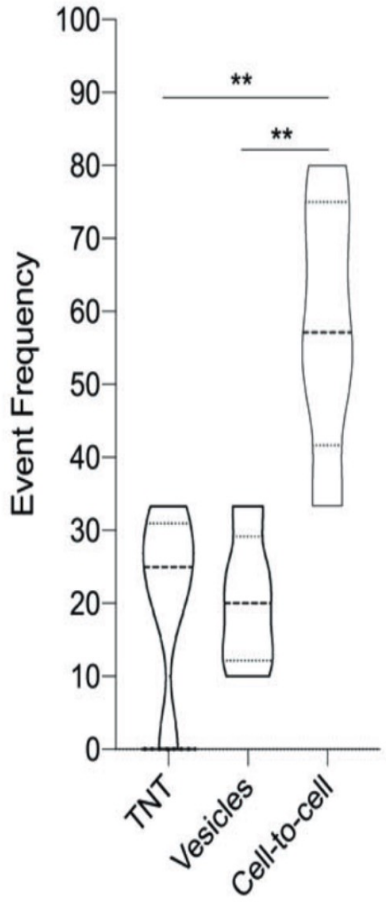




Giallongo C, Oncotarget 2016

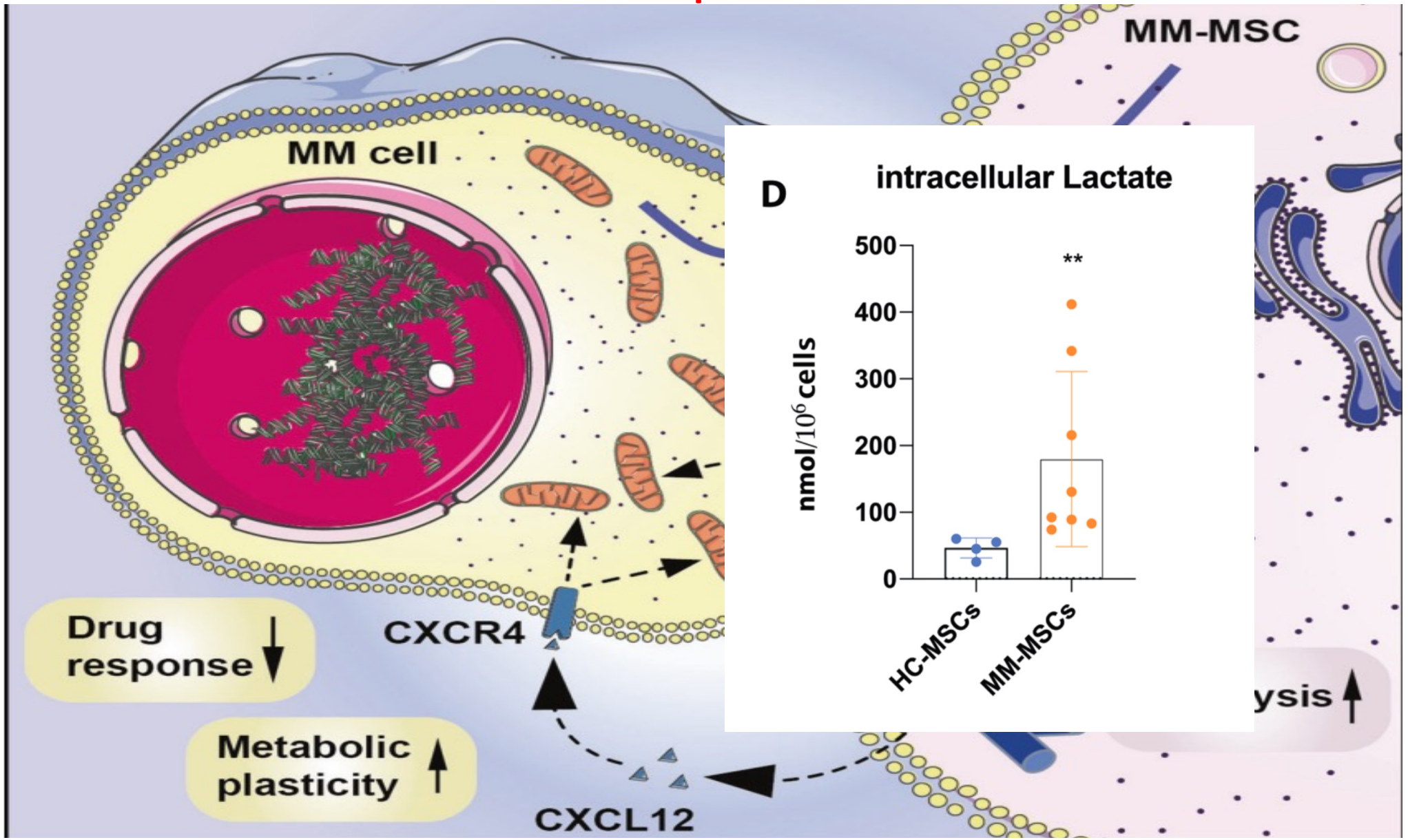
Mitochondria can be transferred from MSCs to U266 cells via TNTs, EVs, or direct cell-to-cell contact



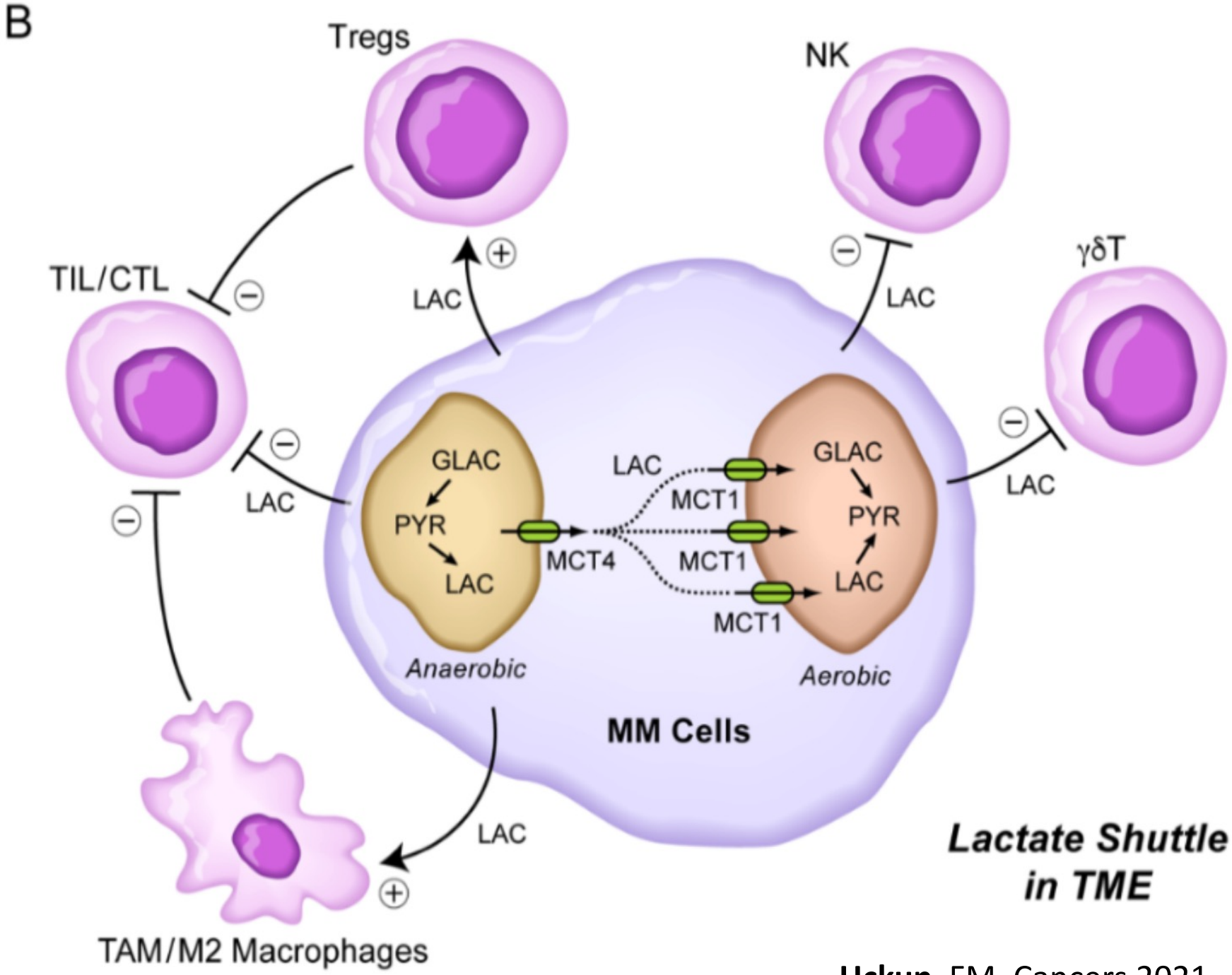


Giallongo C, Oncogenesis 2022

PCs increase the expression of CX43 and CXCL12 proteins in stromal cells with consequent activation of the corresponding receptor CXCR4, which favors mitochondrial uptake from MSCs

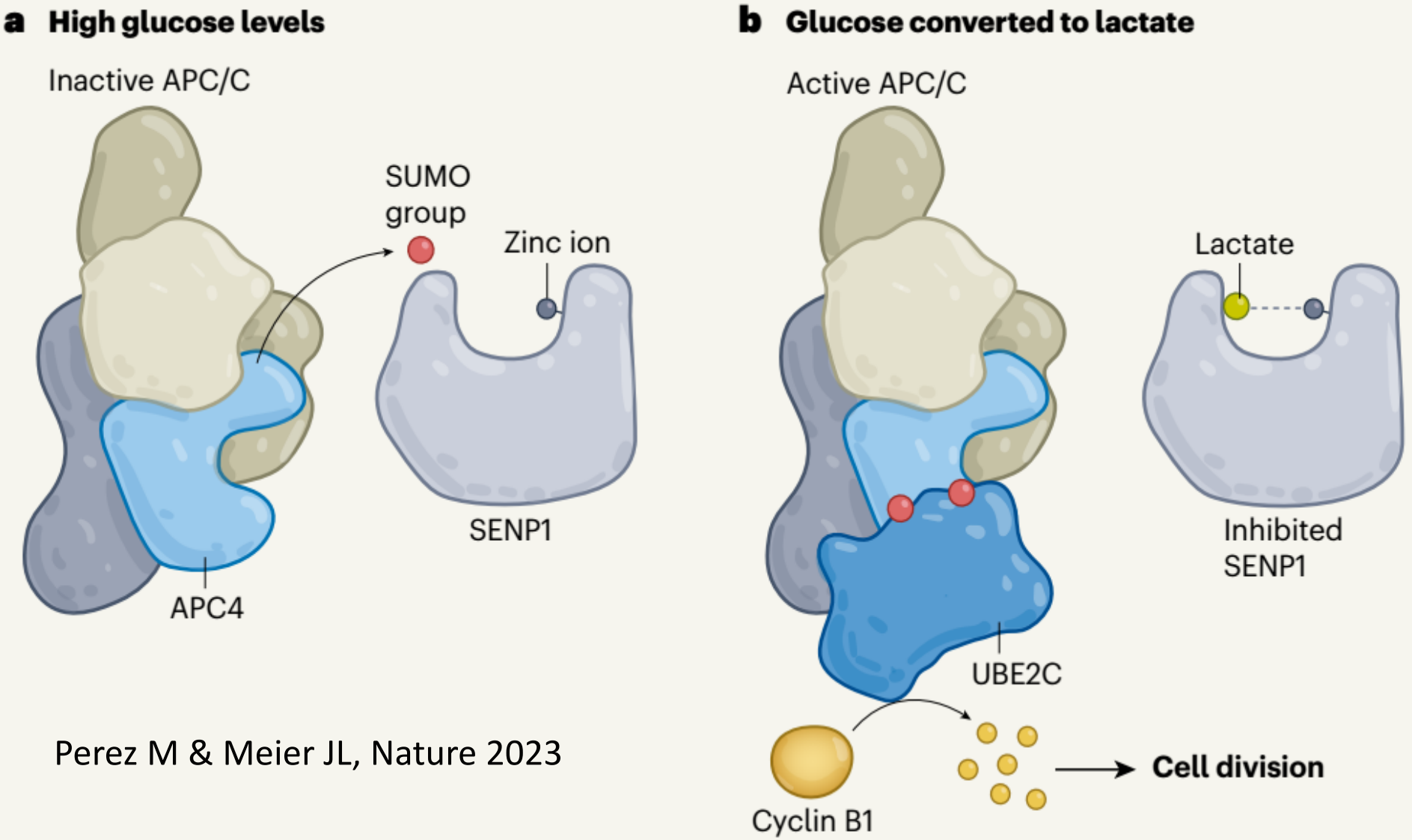


Giallongo C, Oncogenesis 2022



Uckun FM, Cancers 2021

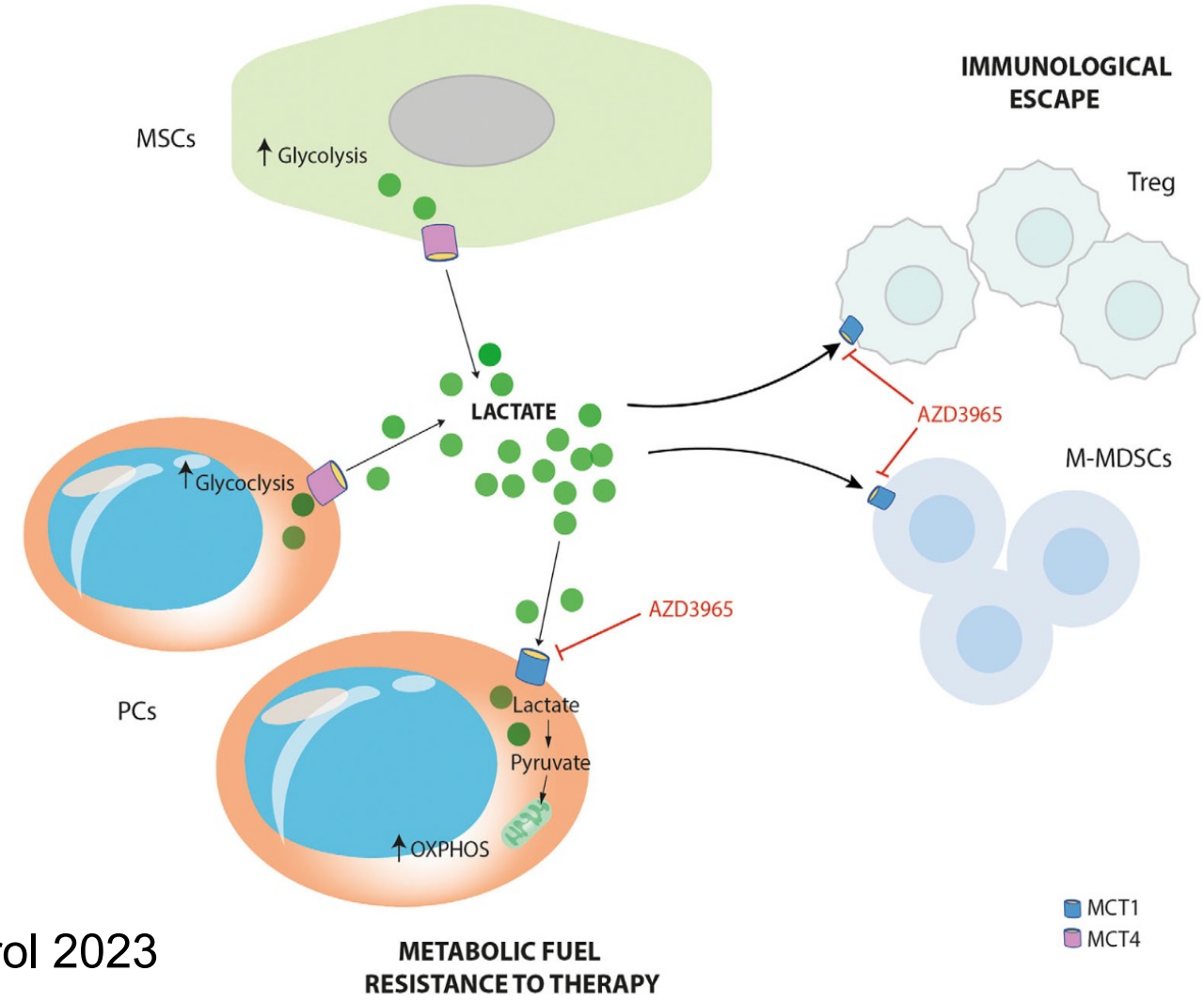
A ‘waste product’ of the metabolism of sugar facilitates cell division



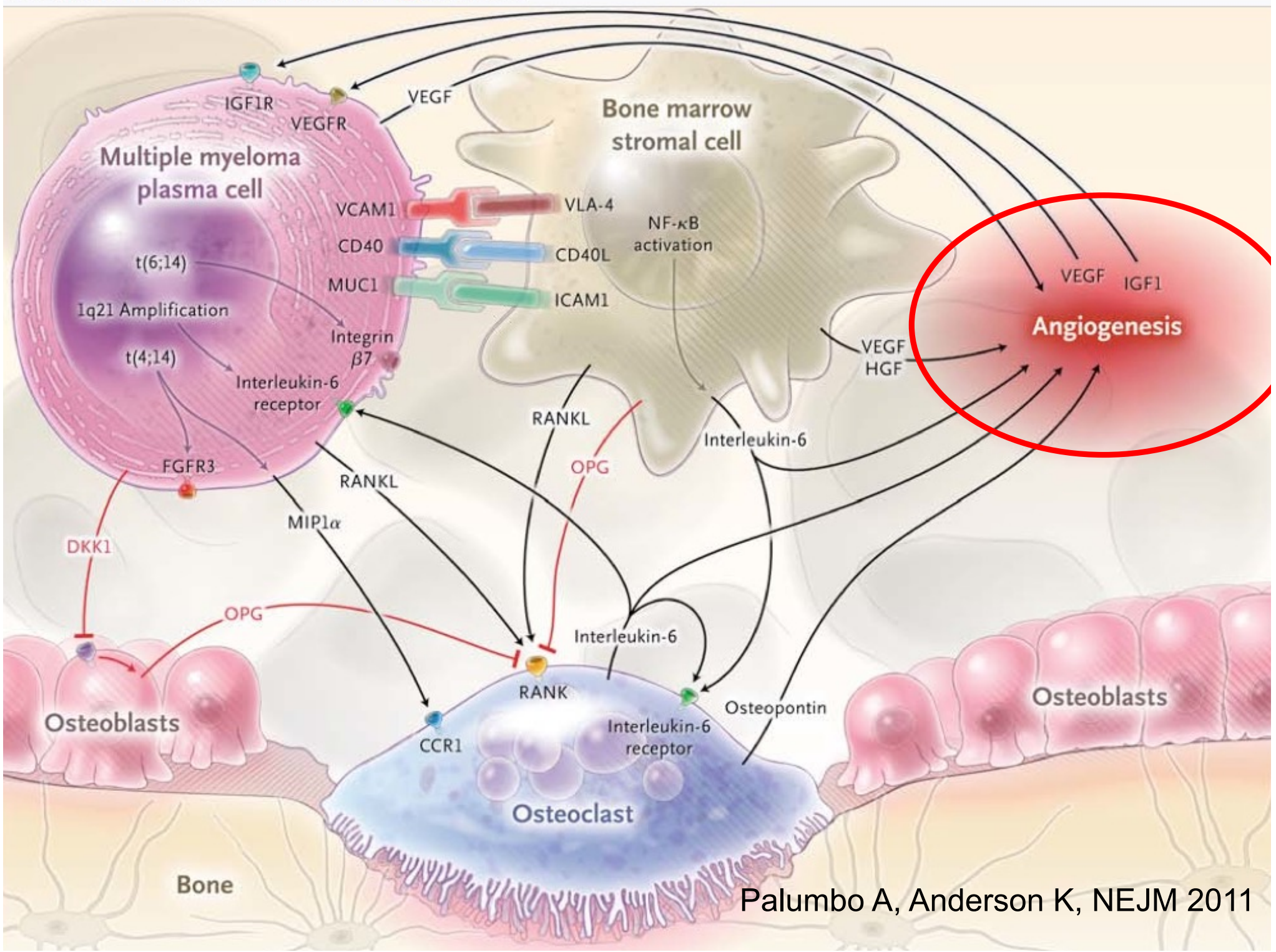
Perez M & Meier JL, Nature 2023

Lactate trafficking inhibition restores sensitivity to proteasome inhibitors and orchestrates immuno-microenvironment in multiple myeloma

FIGURE 6 Lactate trafficking modulates tumour microenvironment in multiple myeloma



Giallongo C. Cell Prol 2023



Palumbo A, Anderson K, NEJM 2011

British Journal of Haematology, 1994, **87**, 503–508

Bone marrow angiogenesis and progression in multiple myeloma

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N Engl J Med 1999

ANTITUMOR ACTIVITY OF THALIDOMIDE IN REFRACTORY MULTIPLE MYELOMA

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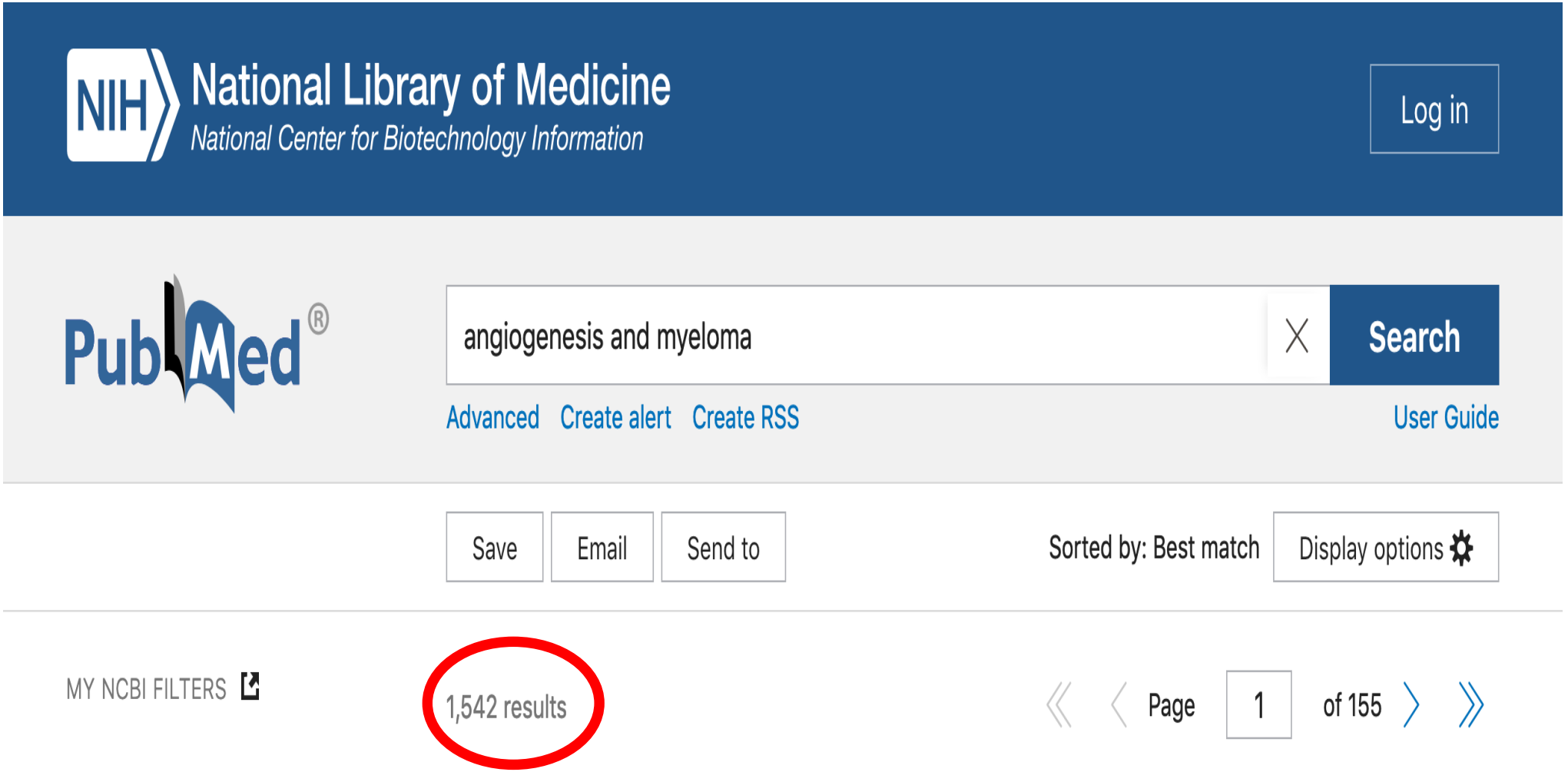
ABSTRACT

Background Patients with myeloma who relapse after high-dose chemotherapy have few therapeutic options. Since increased bone marrow vascularity imparts a poor prognosis in myeloma, we evaluated the efficacy of thalidomide, which has antiangiogenic properties, in patients with refractory disease.

Methods Eighty-four previously treated patients with refractory myeloma (76 with a relapse after high-dose chemotherapy) received oral thalidomide as a single agent for a median of 80 days (range, 2 to 465). The starting dose was 200 mg daily, and the dose was increased by 200 mg every two weeks until it reached 800 mg per day. Response was assessed on the basis of a reduction of the myeloma protein in serum or Bence Jones protein in urine that lasted for at least

MULTIPLE myeloma accounts for approximately 1 percent of all cancers and 10 percent of hematologic cancers. It is incurable with conventional chemotherapy.[1] Melphalan-based high-dose chemotherapy with hematopoietic stem-cell support increases the rate of complete remission and extends event-free and overall survival.[2-4] However, many patients still relapse, and options for salvage therapy are limited.[5,6]

Angiogenesis is important in embryogenesis, wound healing, diabetic retinopathy, and tumor progression.[7,8] The immunomodulatory drug thalidomide can inhibit angiogenesis and induce apoptosis of established neovasculature in experimental models.[9,10] For these reasons, angiogenesis-inhibiting drugs such as tha-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