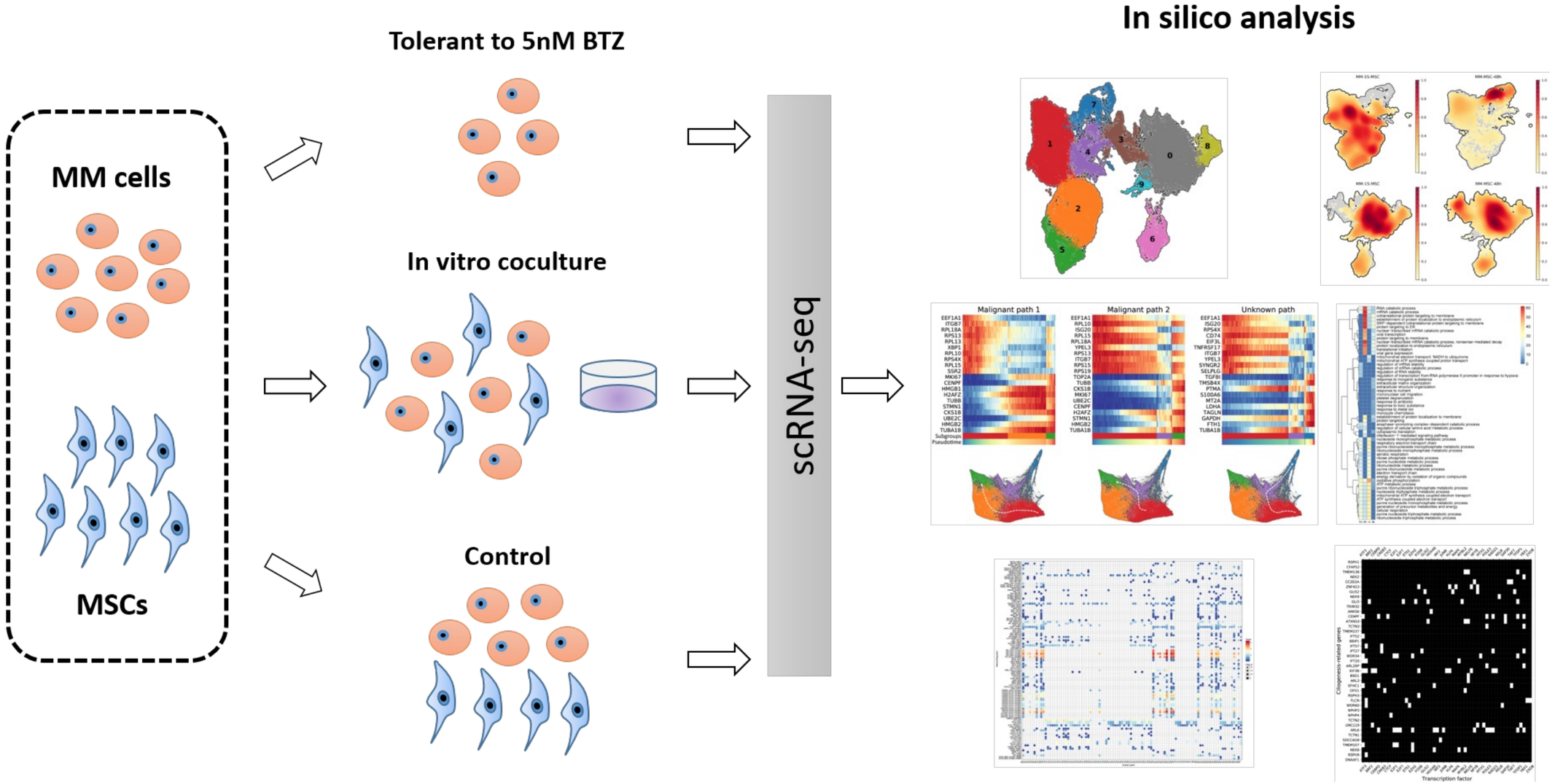
Single-cell transcriptome analysis of interaction between multiple myeloma cells and mesenchymal stem cells



Multiple myeloma (MM) is a cancer of plasma cells, a type of white blood cell that originates in the bone marrow and normally produces antibodies. It accounts for about 13% of hematologic cancers. MM can cause bone pain, anemia, hypercalcemia and renal sufficiency. Bone marrow microenvironment contributes to MM drug resistance, proliferation and migration. Mesenchymal stem cells (MSCs) are multipotent stem cells mainly found in bone marrow and can differentiate into osteoblasts, chondrocytes, myocytes and adipocytes. Recent studies show that MSCs from MM patient are abnormal in both morphology and functions. Some studies show that MSCs support MM growth by secreting cytokines like IL6 while other studies demonstrate that MSCs suppress tumor growth with alleviative bone lesion. Despite extensive research on interactions between MM cells and MSCs, the effects of MSCs on MM growth are controversial and the underlying mechanisms of the interactions remain unclear.

Here, using single-cell RNA sequencing (scRNA-seq), we generate transcriptomes from 25589 intact MM cells and MSCs, transcriptomes from 18934 MM cells that tolerate 5nM Bortezomib (a MM medication) and transcriptomes from 25191 cells co-cultured for 48 hours. We explore potential mechanisms of drug resistance in MM cells and its interactions with MSCs. We find a novel MM cell subtype generated after interacting with MSCs, characteristic with high protein translation and stemness. Further analysis reconstruct transiting trajectories among cell subtypes, identify genes related to MM drug resistance and predict direction-specific ligand-receptor pairs between MM cells and MSCs. Our findings provide insight into interaction between MM and MSCs in bone marrow.