Bone marrow stromal compartment regulates hematopoietic stem and progenitors, and regenerate bone and cartilage. Heterogeneity of this multifunctional microenvironment and distinct physicochemical properties of skeletal system make this compartment particularly difficult to study at a cellular and molecular level. As a result, our fundamental understanding of mesenchymal regeneration and regulation of hematopoiesis has been limited.

To decode this complex environment at the cellular level, we mapped mouse bone marrow stromal cells using multiplexed mass cytometry. First, we generated a cellular atlas, employing markers that have been previously identified in bone marrow stromal cells. Using 16 antibodies simultaneously, we identified 28 distinct cell subsets. Then, we measured levels of cytokines in these subsets as a metric for their contribution to microenvironmental regulation during homeostasis and stress states. This resulted in a multi-dimensional atlas encompassing both homeostatic and diverse stress conditions.

Bone marrow stromal subsets expressing CD73 preserved their cell numbers despite acute radiation stress, whereas CD31−CD105+ populations were particularly vulnerable. Following acute inflammation, modeled by LPS injection, some of the CD31−CD105+ cell subsets had increased levels of TNF-a, IL-3, or IL-6. On the other hand, burn injury caused CD31−CD105+ stromal cells to be depleted, and CD73+ populations to be increased in their numbers. A specific CD73+ population, marked by high level of NGFR, responded to both modes of injury by further increasing its high cytokine levels.

In summary, our work highlighted mass cytometry as a powerful approach to study stromal cell populations across clinically relevant stress states.