University of Rochester

BME PhD Defense Seminar

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MAY 07

Supervised by
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"Taurine Transporter SLC6A6 Expression Promotes Mesenchymal Stromal Cell Function"

Seminar Abstract: Mesenchymal stromal cell (MSC) differentiation is critical for the development, maintenance, and repair of bone tissue. MSCs also play a key role in regulating self-renewal and differentiation of normal hematopoietic and leukemic stem cells. In this work, we analyze multiple murine non-hematopoietic bone marrow single-cell RNA-sequencing datasets and discover that taurine transporter, TauT, expression is enriched in MSCs in vivo.

Although taurine supplements have been shown to mitigate bone defects in aged mice, its role in regulating MSC populations that give rise to bone cells is poorly understood. Using TauT genetic loss-of-function murine models, we find that TauT loss impacts murine MSC populations in vivo and impairs MSC osteogenic differentiation in vitro. This is associated with decreased bone mineral density and bone strength in young and aged TauT knockout mice. Importantly, shRNA-based knockdown of TAUT expression in primary human donor MSCs reduces osteogenic differentiation. TauT null MSCs are unable to support self-renewal and expansion of co-cultured hematopoietic stem and progenitor populations, indicating broad functional defects. Mechanistically, TauT loss results in downregulation of inositol metabolism, increased oxidative stress, and reduced Wnt/β-catenin signaling, which induce MSC senescence.

In addition, our work has identified a key role of taurine produced by bone marrow osteolineage cells in supporting the growth of taurine transporter expressing leukemia cells. Collectively, our data identifies the taurine-taurine transporter axis as a key regulator of MSC maintenance, osteogenic fate determination, and support of normal and malignant hematopoietic cells.

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Zoom: https://rochester.zoom.us/j/99179999015

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