Osteomorphs in Giant Cell Tumor of Bone and Osteosarcoma: Secondary Analysis of Single Cell RNA Sequencing

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INTRODUCTION: Osteomorphs are a recently described and distinct cell type that results from the fission of osteoclasts into smaller daughter cells. Osteomorphs are reported to possess the ability to fuse into osteoclasts in a process known as osteoclast recycling. Previously, it was thought that osteoclasts underwent apoptosis and had a shorter, more limited lifecycle. The presence of osteomorphs and their role in the osteoclast lifecycle has not been described in bone neoplasms. Using previously collected single cell RNA (ScRNA) sequencing, we examined several bone tumors for the presence of osteomorphs.

METHODS: Publicly available scRNA-seq data from the Gene Expression Omnibus for 14 bone tumors were analyzed which included 2 giant cell tumor of bone (GCTB), 5 osteosarcoma (OS), 3 Ewing sarcoma (EWS), and 4 chondrosarcoma (CS). Osteomorphs were defined as cells expressing/upregulating protein coding genes BPGM, FBXO7, AXL, CD74, LEPROT, and CCR3. The selection of these genes was based on previously published findings regarding osteomorph identification and characterization. Uniform Manifold Approximation and Projection (UMAP) was used for dimensionality reduction and visualization of cell types in each tumor using an open-source toolkit for single cell genomics (Seurat v5).

RESULTS SECTION: Likely osteomorph populations were observed in GCTB (1 of 2) and OS (4 of 5) samples. In these samples, the estimated proportion of osteomorphs to all other cells averaged 5.1% (4.8% to 23%). Osteoclast populations in these samples was on average 12% (4.8% to 15.5%). The ratio of osteomorphs to osteoclasts averaged 0.75 (0.375 to 5.04). Presumed osteomorph and osteoclast populations were not identified in the CS or EWS samples, based on a minimum threshold of 2.5% of total cells.

DISCUSSION: Our findings suggest that osteomorphs are present in benign and malignant bone tumors, particularly GCTB and OS. While the clinical implications are still unknown, this study suggests osteomorphs are present in these tumors and should be considered in future studies pertaining to osteoclastic activity in benign and malignant bone tumors.

SIGNIFICANCE/CLINICAL RELEVANCE: This study describes the first osteomorph populations in benign and malignant bone tumors, suggesting that dysregulated osteoclast fission-fusion dynamics may contribute to tumorigenesis or bone destruction. These findings introduce a potential new mechanism in bone tumor biology and highlight osteomorphs as an area of further research.