

## Immune and inflammatory pathways are involved in bone regeneration through inherent bone marrow ossification

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**B**one marrow plays a key role in bone formation, healing, and regeneration. While a subset of marrow explants ossify in vitro without excipient osteoinductive factors, some explants do not undergo ossification. The disparity of outcome suggests a significant heterogeneity in marrow tissue in terms its capacity to undergo osteogenesis. In this study, we sought to identify: (1) proteins and signaling pathways associated with osteogenesis by contrasting the proteomes of ossified and non-ossified marrow explants, (2) temporal changes in proteome and signaling pathways of marrow ossification in the early and late phases of bone formation. Explants of marrow were cultured. Media conditioned by ossified and poorly ossified subsets were collected and proteins unique to each group were identified by proteomic analysis. Proteomic data were processed to assess proteins specific to early phase (Days 1-14) and late phase (Days 15-28) of culture period. Pathways involved in bone marrow ossification were identified via bioinformatics. Twenty-eight proteins were unique to ossified samples and eight were unique to poorly ossified ones. Twelve proteins were expressed during the early phase and fifteen proteins were specific to the late phase. Several identified pathways corroborated those reported for bone formation in the literature. Immune and inflammatory pathways were specific to ossified samples. The marrow explant model indicates the inflammatory and immune pathways to be an integral part of the osteogenesis process. These results align with the clinically reported negative effects of anti-inflammatory agents on fracture healing.

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