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Determining Bone Formation Metabolic Pathway Activity in the TgA86 Mouse Model of Spondyloarthritis through RNA-Seq Data Analysis

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Quantifying metabolic differences through RNA-Seq pathway analysis is vital for understanding spondyloarthritis (SpA). TgA86 mice, overexpressing mouse transmembrane TNF, develop SpA-like features, including joint pathology and new bone formation. We aimed to unveil the underlying mechanism driving spinal bone formation in SpA using RNA-Seq data from TgA86 mice. RNA-Seq datasets from TgA86 vertebrae at 4 and 10 months, and controls, were analyzed. Differential analyses, utilizing whole and immune-associated gene lists, were conducted at the transcriptome level. Metabolomic analyses included comprehensive pathway enrichment and metabolic flux simulations. TgA86 datasets exhibited significant enrichment in lipid-related pathways, particularly phospholipid and nucleotide metabolism. Conversely, mitochondria-associated pathways (oxidative phosphorylation, NAD metabolism) were downregulated. Carnitine shuttle and amino acid metabolism showed significant alterations between the time points. Pattern recognition-based inference of pathogenicity-associated gene clusters validated our pathway analyses. Enhanced activities in specific modules provide crucial insights into SpA pathogenesis, offering potential therapeutic targets. This study advances our understanding of SpA-related bone formation mechanisms, laying the foundation for targeted interventions.