Noble Metal Mineral Ions Direct hMSCs Toward Osteogenic and Chondrogenic Lineages

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Significance: Regenerative medicine techniques involving mesenchymal stem cells (MSCs) utilize a variety of biomaterials to aid in directing differentiation. Noble metal mineral-based bulk and nanostructure constructs are one such class of biomaterials which has been found to influence stem cell fate. For example, gold (Au) nanospheres and rods have been utilized for their significant induction of osteogenic differentiation. However, whole-throughput analysis of noble metals in their mineral-ion form has not been performed to elucidate individual biochemical effects on hMSC modulation and differentiation, representing a critical knowledge gap in biomaterial-directed therapeutics.

Methodology: We evaluated gold (Au), silver (Ag), copper (Cu), titanium (Ti), tantalum (Ta), and platinum (Pt) to determine individual influence on hMSC differentiation. Whole transcriptome sequencing (RNAseq) was leveraged to elucidate key biochemical targets contributing to observed changes in the amplified expression profile. Additionally, complementary in vitro functional studies were performed to visualize and quantify noble metal mineral influence within 2D and 3D culture environments, thus validating cellular modulation via lineage-specific protein staining and RT-qPCR analysis.

Results: Noble metal minerals significantly influence hMSC differentiation, as demonstrated by ion-specific increases in alkaline phosphatase (ALP) activity, matrix mineralization, glycosaminoglycan (GAGs), and aggrecan production. Additionally, RNAseq analysis reveals widespread changes in expression following ion-specific treatment, and identifies biochemical pathways leading to early lineage-specific induction. Further, cellular uptake studies using Western blotting validated key mechanistic pathways discovered by genomic analysis. This study is paramount to elucidating mechanisms of biomaterial-directed stem cell differentiation with limited or no growth factors, which will improve future regenerative medicine outcomes.