Objectives: To examine the effect of Insulin-like growth factor (IGF-I), Platelet-derived growth factor (PDGF), and a combination of PDGF and IGF-I on the in vitro expression of bone and cementum-associated molecules by primary cultures of cells derived from the periodontal ligament (PLF), regenerating periodontal tissue (RTF) and osteoblasts (OB). Methods: Three primary cell types (PLF, RTF and OB) derived from three patients were exposed to the various growth factors for 72hrs, one, three and six weeks. Real time PCR was utilized to quantify the expression of bone markers: bone sialoprotein (BSP), osteocalcin (OCN), Runx2, and cementum markers: cementum attachment protein (CAP), cementum protein-1 (CEMP-1), F-spondin (SPON). Results: Whilst there was some heterogeneity in the expression of markers in the same cell type, IGF-I was found to be the most effective growth factor able to differentiate PLF, RTF and OB cells along a bone tissue producing phenotype, followed by the combination of IGF-I and PDGF. PDGF however was the most effective growth factor in upregulating differentiation along a cementum tissue producing phenotype followed by the combination of IGF-I and PDGF. Osteoblasts were found to be the most responsive cell type to all growth factor treatments followed by PLF. The response by RTF cells was more variable. Conclusion: IGF-I and PDGF were shown to have the potential to differentiate cells derived from the periodontium along either a bone or cementum phenotype.