any bone morphogenetic proteins (BMP). Si and Ca were the primary dissolution products of 45S5 Bioglass. For the concentration range of 15–30 ppm Si and 60–90 ppm Ca, osteostimulation could be observed. Bioactive glass particles are released slowly over weeks and subsequently fill the bone defect by proliferation of osteogenic precursor cells. Osteogenic precursor cells generate ECM proteins like type I collagen via mature osteoblasts. Kaufmann et al. (Kaufmann et al., 2000), observed expression of osteocalcin, osteonectin, and osteopontin genes in osteoblast like cells along with enhanced alkaline phosphatase (ALP) activity. Silver et al. (Silver et al., 2001) observed enhanced Ca concentration in osteoblast cells. In addition to this, ATP generation also boosted up after incorporation of 45S5 Bioglass to the culture medium. For another composition, $50SiO_2$-16CaO-$6P_2O_5$-$5K_2O$-$2Al_2O_3$-1MgO (mol%), increased sulfur and phosphorous concentration could be observed due to the protein content and phosphorylation state, respectively (Laquerriere et al., 2003).

6.7 GENE EXPRESSION/REGULATION BY BIOACTIVE GLASSES

It has been reported by many researchers that bioactive glasses activate the genes associated with bone formation (Jell and Stevens, 2006; Christodoulou et al., 2005). Hench (2009) performed several experiments demonstrating the effect of ionic dissolution products on the specific gene expression for osteoblasts obtained from the excised heads of five individual patients. The experiments showed enhanced proliferation and differentiation of osteoblasts without addition of any bone growth proteins such as BMP and dexamethasone. In addition to this, mineralization of the matrix and generation of ECM proteins could be seen.

Table 6.1 describes the upregulation and activation of seven families of genes when the human primary osteoblasts were exposed to the chemical extracts of 45S5 Bioglass. There was an increase up to 200%–500% in the gene expression over the control culture. The gene expression of bioactive glasses is influenced by four main mechanisms that is, surface topography, chemistry, shear stress at implant interfaces, and nature/type of dissolution ions. Table 6.2 illustrates the gene expression response to Bioglass for various (Jell and Stevens, 2006) bone and cartilage genes. Most of the gene expressions have been studied for osteoblasts, fetal osteoblasts (FOB), human osteoblasts (HOB), fetal chondrocyte (FC), and VEGF (vascular endothelial growth factor). VEGF promotes angiogenesis and ALP provides phosphate, which is required for calcification.

Ferraz et al. (2016) evaluated 23,794 genes for BioS-2P and 45S5 glasses. Osteoblast grown on BioS-2P revealed the downregulation of 11 genes and upregulation of 15 genes, as compared to the control. For 45S5 glass, 21 genes were downregulated and 25 were upregulated as compared to the control. BioS-2P (23.75 Na_2O-23.75 CaO-48.5 SiO_2-$4P_2O_5$) and 45S5 (24.5 Na2O-24.5 CaO-$45SiO_2$-$6P_2O_5$) exhibit composition similarity, due to which