In pre-clinical models, the technology supporting Biomet Bone Healing products has been shown to influence multiple growth factors.²⁶
### Growth Factors are thought to have important regulating effects for bone remodeling and bone healing.\(^1, 26\)

<table>
<thead>
<tr>
<th>Growth Factors</th>
<th>Primary Function</th>
<th>Biomet PEMF</th>
<th>Biomet CC</th>
<th>OrthoFix PEMF</th>
<th>DJO CMF</th>
<th>Exogen LIPUS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMP-2 (Bone Morphogenetic Protein-2)</strong></td>
<td>BMP-2 promotes bridging of callus, and stimulates mesenchymal cell differentiation to an chondroblastic lineage.(^3)</td>
<td>9</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>BMP-4 (Bone Morphogenetic Protein-4)</strong></td>
<td>BMP-4 has been found to play a critical role in the differentiation of mesenchymal cells.(^2)</td>
<td>9</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>BMP-5 (Bone Morphogenetic Protein-5)</strong></td>
<td>BMP-5 influences the generation of osteoclasts.(^3)</td>
<td>9</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>BMP-6 (Bone Morphogenetic Protein-6)</strong></td>
<td>BMP-6 initiates osteoblast differentiation.(^2)</td>
<td>9</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>BMP-7 (Bone Morphogenetic Protein-7)</strong></td>
<td>BMP-7 creates an environment in which stem cells multiply prior to differentiation.(^2)</td>
<td>9</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>TGF-β1 (Transforming Growth Factor-Beta)</strong></td>
<td>TGF-β1 promotes blood vessel formation.(^4)</td>
<td>10</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>FGF-2 (Fibroblast Growth Factor-2)</strong></td>
<td>FGF-2 is associated with an increase in mesenchymal cells, and the differentiation of these cells into chondrocyte and osteoblasts.(^5)</td>
<td>11</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>VEGF (Vascular Endothelial Growth Factor)</strong></td>
<td>VEGF induces angiogenesis, regulates vasculogenesis, and is important in the conversion of soft to hard callus.(^6)</td>
<td>11</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>PGF2 (Prostaglandin E2)</strong></td>
<td>PGF2 accelerates fracture remodeling by increasing the number and activity of osteoclasts, stimulating the proliferation of osteoprogenitor cells, and recruiting osteoblasts from their precursors.(^7)</td>
<td>12</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>IGF (Insulin-like Growth Factor)</strong></td>
<td>IGF-2 enhances BMP-2-induced chondroblast ossification(^8)</td>
<td>18</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

*The absence of a check mark means that there are no data available as of August 1, 2011 indicating the presence of the subject growth factor.*

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\(^11\) Tepero CM, Chang E, Bhatnagar S, Gills JA, Bhatt KA, Hopper RA, Heitman DF, Simon BJ, Gan JC, Loehe JP, and Gurtner GC. Electromagnetic fields increase in vitro and in vivo angiogenesis through a FGF-mediated VEGF independent mechanism. Submitted to FAEB.


\(^15\) Theoretical depiction of the bone healing process.


\(^18\) Heitman DF, Bhatnagar S, Gills JA, Bhatt KA, Hopper RA, Simon BJ, Gan JC, Loehe JP, and Gurtner GC. Electromagnetic field increases in vitro and in vivo angiogenesis through a FGF-mediated VEGF independent mechanism. Submitted to FAEB.


\(^22\) Theoretical depiction of the bone healing process.

