

# GROWTH FACTORS KNOWN TO REGULATE SOFT TISSUE HEALING



The following list of growth factors and cytokines are known to be present within AmnioFix® including some of the most notable: transforming growth factors alpha and beta (TGF- $\alpha$ & $\beta$ ), basic fibroblast growth factor (bFGF), platelet derived growth factors (PDGF AA & BB), and vascular endothelial growth factor (VEGF).<sup>1,3</sup> The growth factors have been quantified and converted to a (+) rating system to provide relative amounts present in the tissue.

REGULATORS OF SOFT TISSUE HEALING IN AMNIOFIX® 1,2,3			
Abbreviation	Cytokine	Function	Content
Ang	Angiogenin	Stimulates migration, proliferation, and vessel formation by endothelial and smooth muscle cells	++++
Ang-2	Angiopoietin-2	Regulates neovascularization in conjunction with angiopoietin-1 and VEGF	+++
bFGF	Basic Fibroblast Growth Factor	Heparin-binding protein with broad mitogenic activity; Potent stimulator of angiogenesis	+++
BMP-5	Bone Morphogenetic Protein 5	Plays a role in bone and cartilage development	+++
BDNF	Brain-Derived Neurotrophic Factor	Supports the growth, differentiation, and survival of neurons	+++
EG-VEGF	Endocrine Gland-Derived Vascular Endothelial Growth Factor	Stimulates endothelial cell migration, proliferation, and survival; Potent stimulator of angiogenesis	++++
EGF	Epidermal Growth Factor	Stimulates proliferation, differentiation, and survival in numerous cell types, including epithelial cells	+++
FGF-4	Fibroblast Growth Factor 4	Broad mitogenic and cell survival activity	++++
KGF; FGF-7	Keratinocyte Growth Factor	Promotes proliferation and migration of epithelial cells and keratinocytes	++++
GH	Growth Hormone	Stimulates body growth through IGF-1 production, involved in anabolic activity	+++
HB-EGF	Heparin Binding EGF-Like Growth Factor	Causes keratinocytes and fibroblasts to migrate to the wound and proliferate; Promotes angiogenesis	++
HGF	Hepatocyte Growth Factor	Regulates cell growth, cell motility, and morphogenesis in epithelial cells; Important in angiogenesis	++++
IGF-1	Insulin-Like Growth Factor 1	Stimulates body growth through broad mitogenic activity	+++
IGFBP-1	Insulin-Like Growth Factor Binding Protein 1	Binds and stabilizes IGF-1 as a carrier protein; Alters interactions with surface receptors	+++++
IGFBP-2	Insulin-Like Growth Factor Binding Protein 2	Binds and stabilizes IGF-1 as a carrier protein; Alters interactions with surface receptors	+++++
IGFBP-3	Insulin-Like Growth Factor Binding Protein 3	Binds and stabilizes IGF-1 as a carrier protein; Alters interactions with surface receptors	+++++
IGFBP-4	Insulin-Like Growth Factor Binding Protein 4	Binds and stabilizes IGF-1 as a carrier protein; Alters interactions with surface receptors	+++++
IGFBP-6	Insulin-Like Growth Factor Binding Protein 6	Binds and stabilizes IGF-1 as a carrier protein; Alters interactions with surface receptors	+++++
$\beta$ -NGF	Beta Nerve Growth Factor	Important for growth, maintenance, and survival of neurons	++
PlGF	Placental Growth Factor	Stimulates proliferation and migration of endothelial cells; Potent stimulator of angiogenesis	+++
PDGF-AA	Platelet-Derived Growth Factor AA	Stimulates proliferation, migration, and angiogenesis	++++
PDGF-BB	Platelet-Derived Growth Factor BB	Stimulates proliferation, migration, and angiogenesis	++++
TGF- $\alpha$	Transforming Growth Factor Alpha	Stimulates proliferation and migration of keratinocytes; Potent stimulator of angiogenesis	++
TGF- $\beta$ 1	Transforming Growth Factor Beta 1	Controls proliferation, differentiation, and apoptosis of numerous cell types	++++
VEGF	Vascular Endothelial Growth Factor	Stimulates endothelial cell migration and activation; Potent stimulator of angiogenesis	+++
TIMP-1	Tissue Inhibitor of Metalloproteinase 1	Binds and inactivates a number of matrix metalloproteinases (MMPs)	+++++
TIMP-2	Tissue Inhibitor of Metalloproteinase 2	Binds and inactivates a number of matrix metalloproteinases (MMPs)	+++++
TIMP-4	Tissue Inhibitor of Metalloproteinase 4	Binds and inactivates a number of matrix metalloproteinases (MMPs)	++++



AmnioFix® dehydrated Human Amnion/Chorion Membrane (dHACM) allografts are processed through the proprietary PURION® Process that provides an effective and easy to use graft while allowing for storage at ambient conditions. AM183.001



**CYTOKINES FOUND IN AMNIOFIX®** Some of the specialized cytokines and proteins found in PURION® Processed dHACM known to regulate inflammation include: Interleukin 1 receptor antagonist (IL-1ra), Interleukin 4 (IL-4) and Interleukin 10 (IL-10), which may be contributing factors to the immunologically privileged properties of the tissue.<sup>1,2,3</sup>

<b>REGULATORS OF INFLAMMATION IN AMNIOFIX® 1,2,3</b>			
<b>Abbreviation</b>	<b>Cytokine</b>	<b>Function</b>	<b>Content</b>
GCSF	Granulocyte Colony-Stimulating Factor	Stimulates the proliferation, differentiation, survival, and activation of neutrophils	++
GM-CSF	Granulocyte Macrophage Colony-Stimulating Factor	Stimulates production of granulocytes and monocytes	+
GDF-15	Growth Differentiation Factor 15	Regulates inflammatory and apoptotic pathways in injured tissues	++++
IFN $\gamma$	Interferon Gamma	Activator of macrophages	++
IL-1 $\alpha$	Interleukin 1 Alpha	Activates lymphocyte proliferation; Induces fibroblast proliferation	+++
IL-1 $\beta$	Interleukin 1 Beta	Involved in lymphocyte proliferation, differentiation, and apoptosis	+++
IL-1ra	Interleukin 1 Receptor Antagonist	Antagonist of IL-1 signaling	++++
IL-4	Interleukin 4	Stimulates proliferation of activated B cells and T cells	++
IL-5	Interleukin 5	Regulates eosinophil growth and activation; Stimulates B cell growth; Increases immunoglobulin secretion	++
IL-6	Interleukin 6	Stimulates production of neutrophils and growth of B cells	+++
IL-7	Interleukin 7	Stimulates proliferation, maturation, and survival of B cells, T cells, and natural killer cells	++
IL-10	Interleukin 10	Enhances B cell survival, proliferation, and antibody production	++
IL-12p40	Interleukin 12 p40	Subunit of IL-12p70; Can act as IL-12 antagonist	+++
IL-12p70	Interleukin 12 p70	Stimulates growth and differentiation of T cells and natural killer cells	+
IL-15	Interleukin 15	Stimulates proliferation of T lymphocytes; Induces proliferation of natural killer cells	++
IL-17	Interleukin 17	Increases chemokine production	++
MCSF	Macrophage Colony-Stimulating Factor	Involved in proliferation, differentiation, and survival of monocytes and macrophages	+++
OPG	Osteoprotegerin	Soluble decoy receptor that inhibits osteoclast activation	++++
<b>Abbreviation</b>	<b>Chemokine</b>	<b>Function</b>	<b>Content</b>
BLC	B Lymphocyte Chemoattractant (CXCL13)	Selectively chemotactic for B lymphocytes	+++
Eotaxin-2	Eotaxin 2	Induces chemotaxis in eosinophils and T lymphocytes	++
I-309	Chemokine Ligand 1 (CCL1)	Recruits monocytes, natural killer cells, and immature B cells and dendritic cells	+++
IL-8	Interleukin 8	Induces chemotaxis in neutrophils and other granulocytes	+++
IL-16	Interleukin 16	Chemoattractant for CD4+ cells, including T cells, monocytes, eosinophils, and dendritic cells	+++
MCP-1	Monocyte Chemotactic Protein 1 (CCL2)	Recruits monocytes, memory T cells, and dendritic cells	++++
MIG	Monokine Induced by Gamma Interferon (CXCL9)	Chemoattractant for T cells	++++
MIP-1 $\alpha$	Macrophage Inflammatory Protein 1 Alpha (CCL3)	Chemotactic for neutrophils and monocytes	+++
MIP-1 $\beta$	Macrophage Inflammatory Protein 1 Beta (CCL4)	Chemoattractant for natural killer cells and monocytes	+++
MIP-1d	Macrophage Inflammatory Protein 1D (MIP-5, CCL15)	Chemoattractant for neutrophils, monocytes, and lymphocytes	+++
RANTES	Regulated on Activation, Normal T-cell Expressed and Secreted (CCL5)	Chemotactic for T cells, eosinophils, and basophils	++++

1. Koob, et al. Int Wound J. 2013;10(5):493-500. 2. Koob, et al. J Biomed Mater Res B – Appl Biomater. 2014; 102(6):1353-1362.

3. Koob, et al. Vasc Cell. 2014; 6:10.