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Organogenesis
NuShield®
Sterilized, Dehydrated Placental Allograft

Preserving All Native Layers Matters

Amnion Layers

Epithelium – Contains higher levels of specific growth factors/cytokines than other layers.[6] Also a rich source of mesenchymal stem cells (MSCs).[7, 8]

Basement membrane – Composed of collagens and noncollagenous glycoproteins.[4]

Compact layer – Forms the main fibrous structure of the amnion.[9]

Fibroblast layer – Thickest layer of amnion and consists of fibroblasts embedded in loose collagen network.[4]

Intermediate (spongy) layer – Contains higher levels of specific growth factors than other layers.[10] Also an abundant source of hydrated proteoglycans, Type III collagen, TGF-ß1, HGF, and hyaluronic acid, which have been shown to be beneficial in the wound-healing process.[6-8]

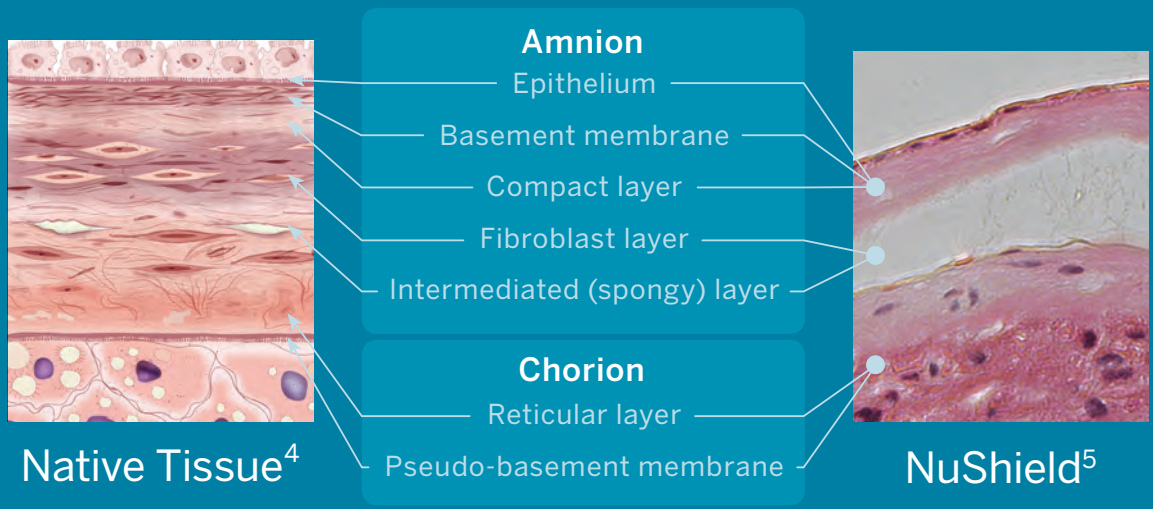
Chorion Layers

Contain growth factors and cytokines[9]

Reticular layer – Composed of collagens and forms the majority of the chorion's thickness,[4, 11] which results in a thick graft with easy handling characteristics.[12]

Basement membrane – Anchors trophoblasts to the reticular layer with collagen IV, fibronectin, and laminin.[4, 11]

NUSHIELD RETAINS ALL NATIVE LAYERS



Support Wound Healing with NuShield®

NuShield is a sterilized, dehydrated placental allograft designed to protect and support healing. It offers a complete, convenient, and valuable solution with the versatility you and your patients need.

All Amniotic Products Are NOT the Same

The placental tissues may all start the same, but the final characteristics are impacted by:

1. Which layers are removed?
2. What was the processing & preservation technique?

The NuShield Difference[1-3]

- Retains all Native Layers, including the spongy/intermediate layer
- Extracellular Matrix (ECM) proteins
- Growth factor/cytokine content that are released over time

Choose the More Complete Option

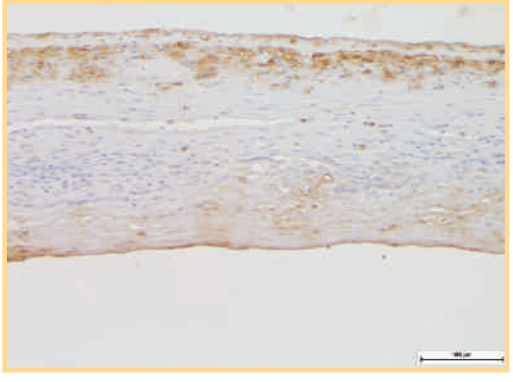
The proprietary process for NuShield preserves the native amnion and chorion with the spongy/ intermediate layer intact, unlike many others on the market.[5, 13]

NuShield also undergoes less manipulation than other dehydrated amniotic allografts.[12]

NuShield also contains key components known to be important in the wound-healing process,[9] including extracellular matrix (ECM) proteins, growth factors and cytokines.

Preserve the Spongy Layer

An *in vitro* study has shown that the NuShield spongy layer contains the following substances:[12]



GROWTH FACTOR, MATRIX PROTEIN	NATIVE FUNCTION
Hyaluronic Acid (HA)	• Component of the ECM[14] • Stimulates cytokine production by macrophages, promoting angiogenesis[14] • Modulate immune responses and reduce inflammatory cytokines[15,16]
Transforming Growth Factor beta 1 (TGF-ß1)	• Granulation tissue formation[17] • Matrix formation and remodeling[17] • Regulate ECM production and degradation[18]
Hepatocyte Growth Factor (HGF)	• Promotion of angiogenesis[19-22] • Keratinocyte migration[23,24]
Interleukin-1 Receptor Antagonist (IL-1ra)	• Completely binds to IL-1 receptors, but does not induce any intracellular response[24] • Knockout of IL-1ra results in reduced angiogenesis, collagen deposition and wound closure[25]

Preserve the Bioactive Factors

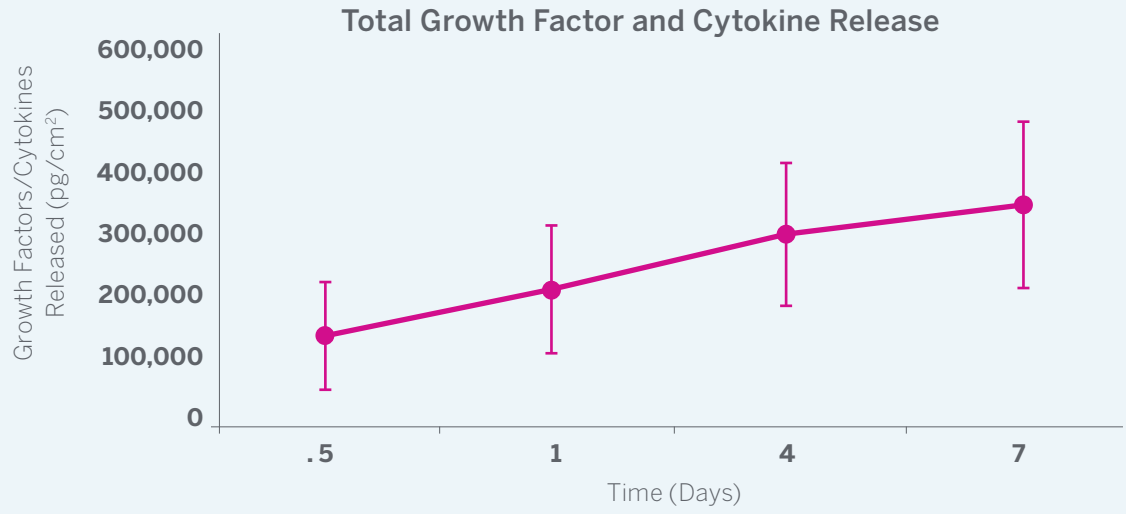
The proprietary process for NuShield preserves numerous growth factors and cytokines with angiogenic, regenerative, and anti-inflammatory properties.

ANGIOGENIC PROPERTIES		REGENERATIVE PROPERTIES		ANTI-INFLAMMATORY PROPERTIES
aFGF	EG-VEGF	Galectin-7	IGF-II	TIMP-1
ANG	PIGF	HGF	PDGF	TIMP-2
ANGPTL4	TSP-1	IGFBP-1	SDF-1	TIMP-4
bFGF	VEGF	IGFBP-5	TGF-ß1	IL-1F5
		IGF-I		IL-1Ra

640 Regulatory Proteins Identified[12]

This is not an exhaustive list.[9]

In Vitro Study Demonstrating the Release of NuShield Growth Factors/Cytokines[12]



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NuShield: True Versatility

Complete to Protect and Support Healing

- The proprietary process for NuShield retains all layers of the native ECM, including the spongy layer

Convenient for All Situations

- 5 year shelf life at room temperature
- Easy-to-use
- Multiple sizes and configurations
- Can be used for various wound types from head to toe, including those with exposed bone and tendon

Assurance of Safety

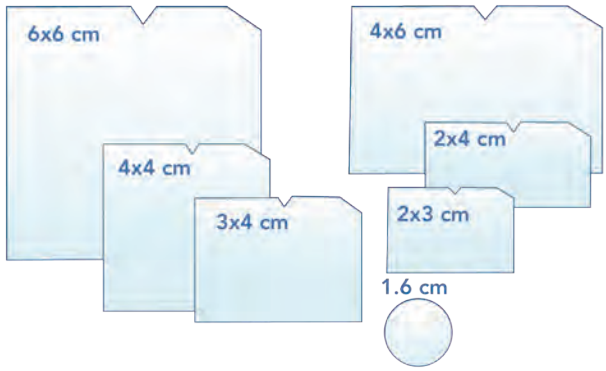
- Donor screening and testing per FDA and AATB standards
- Aseptically processed per FDA and AATB standards
- Terminally sterilized with a Sterility Level Assurance (SAL) of 10^{-6}

Added Value with Added Support

- Reimbursed by CMS as a skin substitute in the high bundle
- Supported by a wide range of customer programs and services

NUSHIELD PRODUCT INFORMATION			
Code	Sizes	Total cm^2	UPC #
NO-1160c	1.6 cm disc	1.6	857877005160
NO-1230	2 x 3 cm	6	857877005047
NO-1240	2 x 4 cm	8	857877005184
NO-1340	3 x 4 cm	12	857877005207
NO-1440	4 x 4 cm	16	857877005054
NO-1460	4 x 6 cm	24	857877005061
NO-1660	6 x 6 cm	36	857877005078

**HCPCS for all NuShield Sizes Q4160*



REFERENCES

1. Mowry KC et al. Novel processing techniques to preserve tissue structure and integrity of amniotic membrane and a comparison to dehydrated amnion-chorion grafts in a rodent animal model. Poster presented at SAWC, Fall 2015
2. Koob TJ et al. Properties of dehydrated human amnion/chorion composite grafts: Implications for wound repair and soft tissue regeneration. 2014. J Biomed Mater Res Part B 2014:102B:1353–1362
3. Data on file. Organogenesis Inc.
4. McQuilling JP et al. Proteomic Comparison of Amnion and Chorion and Evaluation of the Effects of Processing on Placental Membranes. Wounds. 2017;29(5):E36-E40
5. Cooke M et al. Comparison of cryopreserved amniotic membrane and umbilical cord tissue with dehydrated amniotic membrane/chorion tissue. J Wound Care. 2014;23 (10);465- 476
6. Johnson A et al. Response to letter Understanding the impact of preservation methods. Ann Plast Surg. 2017 Apr 12 [Epub ahead of print].
7. Brantley JN, Verla TD. Use of Placental Membranes for the Treatment of Chronic Diabetic Foot Ulcers. Advances in Wound Care. 2015 Vol 4, Iss 9: 545-559.
8. Koizumi N et al. Growth factor mRNA and protein in preserved human amniotic membrane. Curr Eye Res. 2000;20(3):173-177.
9. Niknejad H et al. Properties of the amniotic membrane for potential use in tissue engineering. Eur Cells Mater. 2008;15:88-99.
10. Parolini O et al. Concise Review: Isolation and Characterization of Cells from Human Term Placenta: Outcome of the First International Workshop on Placenta Derived Stem Cells. Stem Cells. 2008;26:300-311.
11. Parry S, Strauss JF III. Premature Rupture of the Fetal Membranes. N Engl J Med 1998; 338:663-670.
12. Hopkinson A. et al. Amniotic Membrane for Ocular Surface Reconstruction: Donor Variations and the Effect of Handling on TGF-β Content. Invest. Ophthalmol. Vis. Sci. 2006;47(10):4316-4322. doi: 10.1167/iovs.05-1415.
13. Bourne G. The Fœtal Membranes. Postgraduate Medical Journal 1962;38:193-201.
14. Schultz et al. (2005). Extracellular matrix: Review of its roles in acute and chronic wounds. World Wide Wounds. 2005.
15. Nakamura K et al. High, but not low, molecular weight hyaluronan prevents T-cell-mediated liver injury by reducing proinflammatory cytokines in mice. J Gastroenterol (2004) 39: 346.
16. Mummert M et al. Synthesis and Surface Expression of Hyaluronan by Dendritic Cells and Its Potential Role in Antigen Presentation. J Immunol 2002; 169:4322-4331
17. Schultz, G. S. and Wysocki, A. (2009), Interactions between extracellular matrix and growth factors in wound healing. Wound Repair and Regeneration, 17: 153-162
18. Sengupta S et al. Hepatocyte growth factor/scatter factor can induce angiogenesis independently of vascular endothelial growth factor. Arterioscler Thromb Vasc Biol. 2003;23(1):69-75
19. Camussi G et al. Angiogenesis induced in vivo by hepatocyte growth factor is mediated by platelet-activating factor synthesis from macrophages. J Immunol February 1, 1997, 158 (3) 1302-1309
20. Grant DS et al. Scatter factor induces blood vessel formation in vivo. PNAS March 1, 1993. 90 (5) 1937-1941
21. Rosen EM et al. HGF/SF in angiogenesis. Ciba Found. Symp. 212 (1997) 215- 26–9.
22. Conway, K et al. The molecular and clinical impact of hepatocyte growth factor, its receptor, activators, and inhibitors in wound healing. 2006. Wound Repair and Regeneration, 14: 2-10
23. Nusrat et al. (1994). Hepatocyte Growth Factor/Scatter Factor Effects on Epithelia. The Journal of clinical investigation. 93. 2056-65. 10.1172/JCI117200.
24. Arend WP et al. Interleukin-1 receptor antagonist: role in biology, Annu Rev Immunol. 1998;16:27-55.13.
25. Eming SA et al. Inflammation in Wound Repair: Molecular and Cellular Mechanisms, Journal of Investigative Dermatology. 2007 127. 514-25

From Organogenesis, which has a legacy of quality, integrity, and commitment to empowering wound care and cell tissue replacement with the most effective solutions. For product information, technical questions or reimbursement, please call 1-888-432-5232.

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