BioTissue®

Our Heritage

Over 38 Years of
Commitment to Regenerative Healing

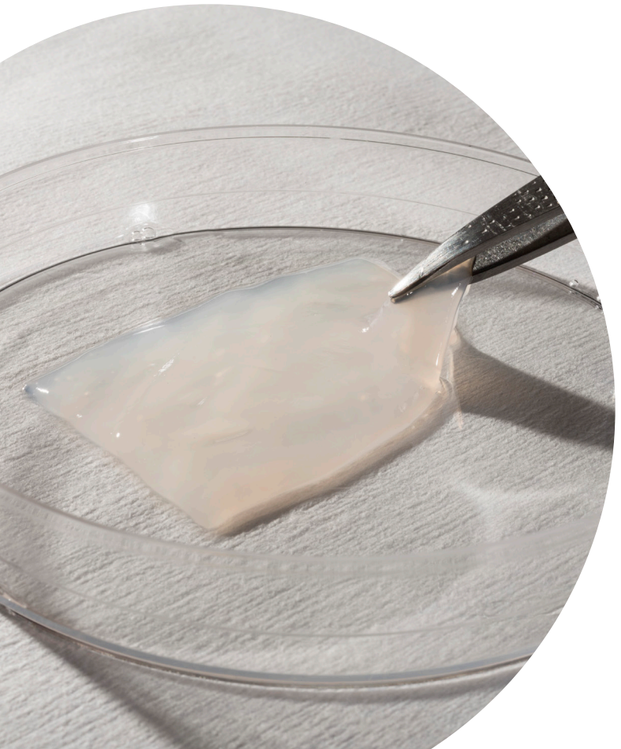
Our Heritage

Where Science Meets Nature

Scheffer Tseng, MD, PhD: ***Co-Founder and Chief Technology Officer, BioTissue***

Our Foundation of Healing

For over 38 years, with continuous support from the NIH and NEI, our work has focused on the improvement of debilitating disease states. Through these efforts, we have identified the potential of human birth tissue in solving many unmet clinical needs and subsequently established Bio-Tissue Inc., the pioneer in the birth-tissue regenerative medicine industry. As an evidence-based leader in technological advancement, we continue to publish our groundbreaking research, with more than 380+ peer-reviewed publications to date.



Where We Started

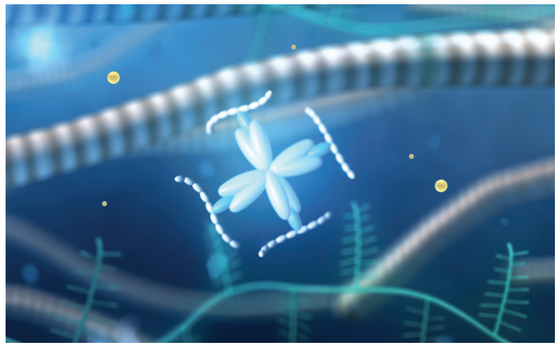
The first reported clinical application of amniotic membrane (AM) was for skin transplantation in 1910; however, it wasn't until 1995 that my colleague J.C. Kim and I reported the use of AM for ocular surface transplantation in a rabbit limbal stem cell deficiency model.[1] We found that glycerin-preserved human AM promoted corneal recovery in rabbits that would sometimes fail with stem cell transplantation alone.

It appeared that the AM acted as a substrate to support the regeneration of corneal epithelium, just as good topsoil in the garden supports the growth of newly-planted seeds. This study suggested—for the first time—that inadequate wound healing lies in the lack of a supporting environment, and AM transplantation can serve as a surrogate niche environment to facilitate regenerative wound healing.

Our Breakthrough Discovery

The therapeutic effect of AM is believed to originate from its innate wound healing, anti-scarring and, most importantly, anti-inflammatory properties. In 2001, when cryopreserved AM received approval for ocular surface reconstruction through Request for Designation from the Food and Drug Administration (FDA), it was recognized to promote healing through anti-inflammatory, anti-scarring, and antiangiogenic effects.

Since that time, my colleagues and I have pondered the following question: What is in birth tissue that is responsible for these amazing results? One may naturally assume that AM's complex actions are likely to be based on a symphony of biological molecules, but our cumulative research over the last decade suggests otherwise. Between 2002 to 2013, our research has focused on isolating the key molecules in birth tissue that contributes to its healing properties. **We successfully identified and purified HC-HA/PTX3,[2] a unique complex naturally present in AM and umbilical cord (UC) that orchestrates multiple anti-inflammatory, anti-scarring and anti-angiogenic effects and plays an important role in promoting regenerative wound healing as evidenced in the ocular segment.[3-9]**



Our Hypothesis

Our research has shown that the anti-inflammatory mechanism of action of birth tissue is through the downregulation of pro-inflammatory innate immune responses by promoting apoptosis of activated neutrophils and macrophages as well as phagocytosis of apoptotic neutrophils by polarizing M2 macrophages.[4] Further, the direct anti-scarring action of AM was supported initially by its ability to downregulate the expression of TGF-β1 in fibroblasts.[5,6] More recently, we discovered that this anti-scarring action based on suppression of canonical TGF-β1 signaling is coupled with reprogramming of corneal fibroblasts and myofibroblasts into keratocytes.[7]

We have also shown that HC-HA/PTX3 maintains stem cell quiescence by upregulating BMP signaling in limbal niche cells, leading to BMP signaling in limbal epithelial cells that reverts limbal niche cells back to their progenitor phenotype.[8] Thus, these collective actions by HC-HA/PTX3 explain the molecular mechanism by which the birth tissue can supplement and support limbal epithelial stem cells by serving as a native niche matrix.[9]

These actions may also explain why HC-HA/PTX3-containing birth tissue, such as Prokera®, has been shown to promote corneal nerve regeneration to support its lasting benefit in managing moderate to severe dry eye[10] and corneal neuropathic pain.[11] The latter has led to TissueTech's receipt of a 5-year NIH RO1 grant (R01NS117761), together with Johns Hopkins Hospital, to investigate birth tissue products as non-opioid alternatives in managing post-surgical pain, promoting nerve regeneration, and dampening peripheral and central sensitization of nociceptive pain stimuli.

Preserving Mother Nature

We have developed a unique processing method (CryoTek®) to preserve HC-HA/PTX3 and growth factors/cytokines from the birth tissue while devitalizing living cells. In contrast, tissues processed via heat dehydration are structurally compromised and contain significantly less of the HC-HA/PTX3 complex.[12,13]

Seeing the Potential

In 2011, our company expanded from ophthalmology into additional markets including orthopedics,[14-16] neuropathy,[17] wound care,[18-23] spine,[24] urology[25] and pain management[26,27] using the same birth tissue products processed using our patented manufacturing technology. Our Neox® and Clarix® allografts are marketed as structural tissue products for homologous use as protective barriers and wound coverings. These products are manufactured and distributed in compliance with the regulatory requirements of 361 HCT/Ps that are regulated solely under section 361 of the Public Health Service Act and 21 CFR Part 1271.

Our Future Journey

BioTissue is pursuing FDA approval through submission of a Biologics License Applications (BLA) for some of its products as evidenced in a recently published Phase 2 study for complex diabetic foot ulcers.[20] Our company will continue to provide sustainable health economic value, solve unmet clinical needs, and lead in technological innovation in seeking to deliver the promise of regenerative healing for our physicians and patients.

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