Beyond Mammalian Tissue:
Exploring the Benefits of Omega3 Rich Fish Skin for Tissue Regeneration

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Disclosure

Paid Consultant
Acelity, Smith & Nephew, Integra, Pluristem, MediWound, Acton, e-Kare, Kerecis, Restorix

Principal investigator
Acelity, Integra, Smith & Nephew, TissueTech, Pluristem

Grant Support
Smith & Nephew, Acelity, Integra

As pertains to this talk: Kerecis
Product Background and History
Product history

- First accounts of skin grafting date back to fifth century India
- Cadaveric skin became very popular, though cumbersome
- Human skin banks operated since 50s
- Price 30 – 90 USD / cm²
- Significant shortages of supply
- Xenograft technologies developed in the 20th century to respond to shortage
- Fish Skin is a proprietary fish skin xenograft
Fish skin – Product overview

- Fish skin for medical use patented by Kerecis™
- Like human skin, fish skin consists of cells embedded in a network of non-living tissue
- Fish skin is FDA cleared
- Proteins and lipids in their natural state
- Decellularized and sterilized
- Non allergenic and bio compatible
How Fish Skin works

Fish skin is harvested from wild Atlantic cod

Cells are removed from the fish skin. Acellular graft remains, rich in omega-3 PUFA

Human cells penetrate the Fish Skin ADG and convert remodel into a new tissue
Basic Science
Why is extracellular matrix (ECM) important? Structural and regulatory role of ECM

- Extracellular matrix (ECM) serves as supporting scaffold for invading cells
- Cell adhesion to ECM is a prerequisite for maximal bioactivity of growth factors
- ECM molecules and growth factors regulate together cellular processes during wound healing
- Fish skin is a xenograft (acellular dermal graft- ADG) that retains the natural ECM structure of the fish dermis
SEM pictures show the similar structure of human and fish dermis in high magnification. Bar 1µm.

Figures:
Fish dermis: Kerecis data on file. 2010
Scanning electron microscopy imaging of Omega3 fish skin and human skin. The key structural features of fish skin and human skin is evolutionary conserved. Scale bar: 100 µm.
Structural comparison of different biological wound materials with scanning electron microscopy. Omega3 fish skin bears most resemblance to human skin structure and contains the ideal pore size (10-100 µm) for cellular ingrowth.
Three Dimensional Cell Ingrowths

- Fibroblast seeding on Omega3 fish skin graft (left) and a human amnion/chorion membrane allograft (right).
- Results show that cells infiltrate and proliferate in the Omega3 Fish graft but not into the human amnion/chorion membrane allograft.
- Negative controls showed no cell staining.
In Vitro and In Vivo Histology

H&E images of cell infiltration into Kerecis from vitro experiments,

From human implants – showing cell infiltration
Ideal Pore size for early cellular population
Fluorescent staining of early cellular population

Cellular population

Negative control
Clinical Research – The Present
Clinical Evidence

- Double blind Randomized Clinical Trial
  - *Journal of Lower Extremity Wounds* – 2015
  - Healthy volunteers
  - Forearm punch model
  - Significantly (p=0.041) faster healing compared to porcine product (Oasis®)
  - No autoimmune reactions
    - ELISA tests on RF, ANA, ENA, anti ds-DNA, ANCA, anti-CCP, and anticollagen I and II.

![Graph showing more healed wounds percentage over days 14, 21, and 25.]
The primary objective was assess the percentage of wound closure area from baseline after 5 weekly ECM applications in 18 patients with at least one “hard to heal” criteria. After eligibility assessment the patients underwent application of the ECM for 5 sequential weeks, followed by 3 weeks of standard of care; secondary wound dressings were applied per their underlying etiology. Wound area, signs of infection and pain were assessed weekly visits.
Clinical Evidence

- **Clinical Trial on 18 patients**
  - A prospective, single-center, non-blinded, non-comparative, post-market compassionate clinical evaluation of a Novel Acellular Fish Skin Graft which contains Omega3 fatty acids, for the closure of hard to heal lower extremity chronic ulcers. 
  - *WOUNDS – 2016* 
  - Thais O. Polanco MD, C. Kevin Yang MD, John C. Lantis II, MD

- 40% decrease in wound surface area was seen with 5 weekly applications (P<0.05)
- Notable reduction pain and drainage
- Concluded that the “fish skin graft is effective treatment for hard to heal lower extremity chronic ulcers, especially where many other products fail”.
Clinical Evidence

Representative Case

Surface area reduction

![Graph showing surface area reduction over weeks](chart.png)
Clinical Evidence

- Retrospective Clinical Trial on 59 patients
- *Symposium on Advanced Wound Care - Fall 2015*
- 87% either improved or healed in 4 weeks. None of the non-responsive wounds got worse.
- No allergic reactions were noted and no parvalbumin was detected
- Less use of antibiotics was noted

<table>
<thead>
<tr>
<th>Wound type</th>
<th>Wounds treated</th>
<th>Improved</th>
<th>Healed</th>
<th>Not responding</th>
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<tbody>
<tr>
<td>Venous or mixed venous/arterial</td>
<td>27</td>
<td>19</td>
<td>6</td>
<td>2</td>
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<tr>
<td>Arterial</td>
<td>7</td>
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<td>2</td>
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<tr>
<td>Diabetic</td>
<td>8</td>
<td>3</td>
<td>4</td>
<td>1</td>
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<tr>
<td>Surgical/Trauma</td>
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<td>5</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Pressure</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td>1</td>
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<tr>
<td>Neuropathy</td>
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<tr>
<td>Other</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Total number of wounds</strong></td>
<td><strong>68</strong></td>
<td><strong>40</strong></td>
<td><strong>19</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>
NOW WITH NEW THOUGHTS…..

• A RELATIVELY CLEAN WOUND
• THAT CAN BE DEBRIDED IN PATIENT OR OUT PATIENT
• THAT NEEDS RAPID RE–EPITHELIAZATION
• VERSUS DEEP TISSUE REGENERATION
• THAT HAS AN INFLAMMATORY / INFECTIOUS COMPONENT
• POTENTIALLY FREQUENT APPLICATIONS…..WEEKLY…
• THANK YOU