

Tobacco Derived Human Collagen for Orthopedics

BY ROBIN YOUNG

Human cadaver or bovine derived collagens are routine additions to many orthopedic procedures. But that could change.

A July 12 announcement from Israeli company CollPlant Ltd. signals that tobacco derived human type 1 collagen is moving into orthopedics. CollPlant received CE Mark for its Verginix WD tobacco plant derived human collagen in 2012. And then earlier this year, the company announced the interim results from two human clinical studies of its tobacco derived collagen.

Could FDA approval and U.S. commercialization be on the near horizon?

Human Collagen From Tobacco

Tobacco is complex and, it turns out, is one of the most exciting new innovations in medicine—successfully tackling the Ebola virus, wound care and surgical orthopedics.

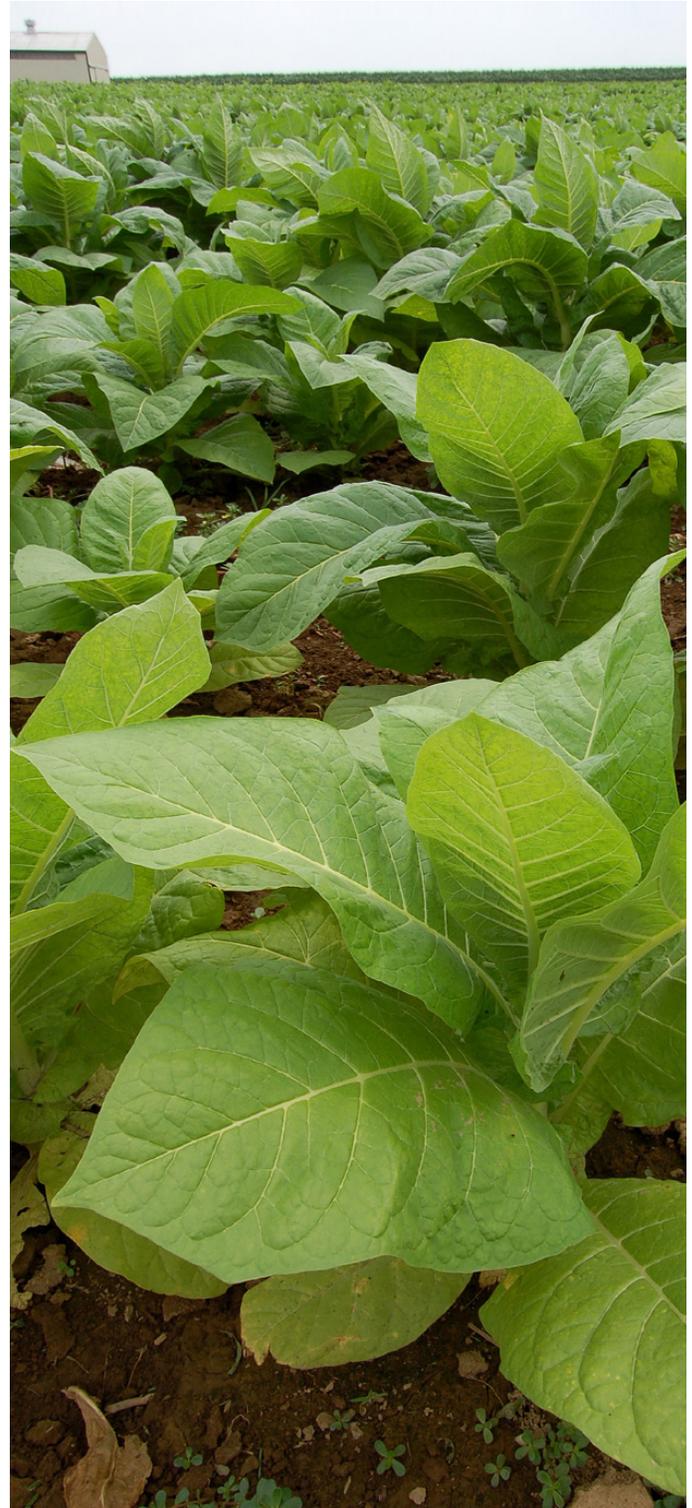
When the Ebola outbreak was at its worst, it was a tobacco derived product that turned out to be the best hope for those desperate patients. As long time *CBS* reporter Bob Simon described in his final story for *60 Minutes* on February 15, 2015, a tobacco grown drug, ZMapp, had successfully treated Ebola patients.

In his dramatic story, Simon interviewed the U.S. doctor who'd contracted the Ebola virus while treating patients in Africa and was then airlifted back to the U.S. and treated with ZMapp. When he arrived in the U.S. he was fighting for his life. Injections of ZMapp, he said, cured him.

ZMapp is produced in Owensboro, Kentucky, by Kentucky Bioprocessing, LLC (which was recently purchased by cigarette giant Reynolds American Inc.) in a tobacco plant greenhouse. The tobacco plants have an ability to produce antibodies to the Ebola virus. Which is amazing. Kentucky Bioprocessing extracts the Ebola antibodies from the plants and produces dosages of ZMapp.

Before ZMapp, however, it was an Israeli professor, Oded Shoseyov, from Hebrew University, who first coaxed transgenic tobacco to express all five essential genes necessary to produce the first medical product from tobacco. For his discoveries, Professor Shoseyov received the Kaye Innovation Award from the Hebrew University Board of Governors.

CollPlant then developed the mass production techniques which allow for the production of large quantities of medical grade, human col-



Wikimedia Commons and Derek Ramsey

lagen. Yissum, the technology transfer company of Hebrew University, is one of the shareholders of CollPlant, an Israeli public company traded under the symbol "TASE."

Why Collagen?

Collagen is a primary building block for the human body and has long been a vital protein in the medical field. Essential for tissue repair, physicians routinely use collagen products in a wide range of bone void fill or soft tissue augmentation procedures as well as treating chronic wounds, burns, or for aesthetic indications. Virtually all medical grade collagen, in whatever form, is presently derived from cadaveric or bovine or porcine sources.

The Tobacco Derived Collagen Difference

Enter tobacco derived human type 1 collagen.

CollPlant derives pure recombinant type 1 human collagen, which starts in tobacco leaves, and purifies the collagen in an extremely complex process to a level suitable for medical implantation.

Among the advantages of CollPlant's approach are:

1. No immunogenic response — Turns out that human collagen produced from genetically modified tobacco does not trigger an immunogenic response.
2. Bioactive — Tobacco extracted recombinant human collagen type I forms thermally stable helical structures and fibrillates. It's bioactivity—as confirmed with its human clinical trials—resembles native human collagen.
3. Very homogenous — Being plant derived, its molecular structure is more "pure" than either cadaveric or xenographic collagen. One theoretical advantage is a shorter patient recovery time.
4. No disease or pathogen transmission.
5. Grows fast — It takes tobacco just eight weeks to grow to harvestable size. Lower prices, higher volumes—in theory.

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Vergenix® WD

The first commercial medical product derived from tobacco derived human collagen is Vergenix WD. It is a collagen-based bandage for treating chronic wounds (diabetic ulcers, venous ulcers, bedsores, poor healing trauma wounds or burns). It was awarded CE Mark for commercialization in Europe and approved by several other countries in 2012.

In the pipeline are products to treat tendonitis, bone voids, spinal fusions and trauma indications.

Clinical Outcomes – So Far

On March 18, 2015 CollPlant announced that 11 out of 20 patients participating in a chronic wound care study had completed their enrollment. Interim results, said the company, showed that 10 patients reported 80%-100% wound closure within four weeks of starting treatment. The study is being conducted in three leading HMO clinics in Israel.

In January 12, 2015 CollPlant announced that it had begun human clinical trials for a tendon repair form of its tobacco derived collagen called, Vergenix STR. The product is intended to be used for patients with tendonitis, specifically “tennis elbow.” The protocol calls for mixing Vergenix with a concentration of platelet-rich-plasma, derived from the patient’s blood, and injecting it one-time at the point of tendon injury.

When the tendonitis study was announced, the company said that it would begin commercializing Vergenix in Europe this year.

Then came last week’s announcement.

Entering the U.S. Market

On July 12, CollPlant announced that it had signed a term sheet to develop and

commercialize a new collagen (tobacco derived, of course) product for spine fusion and trauma indications with an un-named U.S. based partner (can’t be Medtronic—they’re Irish now).

Since the newly signed term sheet is non-binding, both parties to the agreement have decided to keep the identity

of the U.S. company confidential pending negotiation of a final agreement.

But the company, which CollPlant characterized as, “a leading U.S. company in the field of orthobiologics,” would partner with CollPlant to develop and commercialize a new absorbable bio-active surgical matrix

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intended for use in spinal fusion and trauma applications.

The new matrix would be composed of CollPlant's type I recombinant human collagen and synthetic minerals that mimic bone structure. Interestingly, the term sheet would allow for adding in so-called "bio-functional molecules." Stem cells?

According to the press announcement accompanying the term sheet signing, "CollPlant's rhCollagen is identical to the type I collagen produced by the human body, and has significant advantages compared to currently marketed tissue derived collagen, including improved biofunctionality, superior homogeneity, and reduced risk of immune response and transmission of diseases."

Said CollPlant CEO Yehiel Tal: "This agreement represents recognition of the value of our proprietary rhCollagen technology and biomaterials knowhow, and, over time, should help to catapult CollPlant to the forefront of the orthopedic market."

Under the terms of the agreement, if consummated, CollPlant would receive payments for the license to use its technology, milestones for achieving certain clinical and regulatory events and single-digit royalty payments for future global sales, as well as participation in costs associated with the building of a CollPlant-run manufacturing facility for the production of rhCollagen and the product in the U.S.

The agreement is non-binding and may not ultimately result in a definitive agreement.

Tobacco

Tobacco, a uniquely American plant, was used by generations of Native

Americans as offerings to the spirits, for planting, for healings and for ceremonies. Among the many Native American tribes, tobacco was a sacred plant. It represented prayer, protection, respect and healing.

Before it was a recreational drug, tobacco was medicine.

After Europeans migrated to the Americas tobacco became "gold power" and funded the colonies, the clergy and the militia. In 1723 Maryland and Virginia exported thirty thousand kegs per year requiring 200 ships to transport it. It was no accident that tobacco leaves were sculpted into the columns of the capital building in Washington, .DC.

A century later tobacco became synonymous with the destruction of public health.

But, as scientists are now demonstrating, tobacco, perhaps more than any other plant known to science, is well suited for rapid development of a wide variety of valuable medicines and biologics.

Besides CollPlant several companies are developing advanced medicines or biologics by exposing tobacco plants to genetic materials and then extracting vaccines, antibodies or biologic materials.

What is so amazing is tobacco's capability to generate all of these valuable medicines and human biologics in their leaves.

We always thought that tobacco was a drug delivery vehicle. But nothing like this.

Remarkable. ♦

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