

Just A Simple Swab, And No More Cavities

University of Florida



Innovative technologies developed at the University of Florida that can eliminate dental cavities and possibly major bacterial infections have the potential to affect the entire human population.

David Day, director of the Office of Technology Licensing at the University of Florida, boils it down to a simple explanation: “A single swab of the mouth could result in the total elimination of cavities.”

Though the compelling story behind this concept began several decades ago, well before his tenure at the university, Day is now involved with the process that may soon make this treatment a reality. About 15 miles from his office on the Gainesville, FL, campus resides a small biotechnology startup called Oragenics Inc. that is poised to launch two very promising, and potentially revolutionary, products.

The two technologies — Replacement Therapy and Mutacin 1140 — share a common background and are the result of more than 25 years of work by Jeffrey Hillman, D.M.D., Ph.D. Hillman’s research on the action of bacteria that cause tooth decay began at the Forsyth Institute in Boston and continued when he moved to become professor at the University of Florida College of Dentistry.

By the mid-1990s Hillman had conceived of an approach to oust cavity-causing bacteria that take up residence on teeth. The key to the technology's success was to replace the destructive bacteria with a genetically engineered strain of bacteria incapable of causing decay. Once replaced, the decay-causing bugs are virtually powerless to come back.

Hillman worked with the Office of Technology Licensing to obtain an exclusive worldwide license to the technology, named Replacement Therapy. With the help and business expertise of fellow dental researcher Robert Zahradnik, Ph.D., the two colleagues founded Oragenics in 1996. Early growth and development phases moved forward, and less than seven years later the company announced the successful completion of its \$3 million initial public offering.

Envisioning a Global Treatment

Though small in size — Oragenics now has 11 employees — the company continues to grow and change as excitement about its products increases. In September 2005 Zahradnik was named president and chief executive officer of Oragenics; just before that, the company achieved a major milestone as it began a Phase I clinical trial of Replacement Therapy designed to evaluate the safety of the technology. Zahradnik is optimistic and echoes Day when describing the potential impact. “The best way of looking at this technology,” he says, “is that one painless treatment can offer a lifetime of protection.”

“Zahradnik says that to date Oragenics has received \$5 to \$6 million in investments; he also says that investors must view a technology of this nature on a global basis. Indeed, from a public health perspective, Replacement Therapy can address the needs of numerous developing countries and could improve the dental health of 5 billion people worldwide.”

Replacement Therapy has such enormous potential because tooth decay is so prevalent. According to Hillman, tooth decay is the most common chronic infectious disease in the world; essentially everybody has it. Yet at the present time there is nothing available to help prevent tooth decay. Despite the typical hygienic precautions followed by most people for the past 25 years — using fluoridated water, brushing thoroughly and undergoing regular cleanings — tooth decay continues to thrive. In unindustrialized countries where fluoride and cleanings are not readily available, Replacement Therapy could have a tremendous impact.

“Replacement Therapy has a major advantage over these approaches because there is no patient compliance required,” Hillman says. “Replacement Therapy can be done in the dentist's chair. The dentist just swabs the replacement strain (of bacteria) on the patient's teeth for five minutes, and that's all you need to do. When the patient leaves the chair, nothing else will have changed except that the chance of tooth decay and incidence of cavities will be dramatically decreased.”

The science behind Replacement Therapy is based on the fact that most human tooth decay is caused by a naturally occurring bacterium called *Streptococcus mutans*. These bacteria sit on the surface of teeth and convert sugar that we ingest to lactic acid that, when excreted by the bacteria, dissolves the mineral that makes up tooth enamel and dentin. Hillman succeeded in genetically engineering a strain of *Streptococcus mutans* that produces a small amount of antibiotic capable of eliminating all other strains of *Streptococcus mutans*. Moreover, through recombinant DNA

technology, this modified strain can no longer produce lactic acid. Topical application of the patented strain of *Streptococcus mutans* to a person's teeth actually displaces any decay-causing strain of *Streptococcus mutans*. This approach has been described as fighting fire with fire.

Potential Reaches Far Beyond Fighting Cavities

During the course of developing Replacement Therapy, Hillman recognized the tremendous potential of the particular antibiotic he engineered into the replacement strain. A second major focus by Oragenics is Mutacin 1140, a novel broad-spectrum antibiotic peptide that has proven to eliminate some of the most dangerous and stubborn infectious bacterial strains worldwide. In laboratory studies, Mutacin 1140 has demonstrated potency against essentially all gram-positive bacteria and certain medically important gram-negative bacteria including those responsible for strep throat, common pneumonia and staphylococcal infections. In particular, multidrug resistant *Staphylococcus aureus* and *Enterococcus faecalis*, which are notorious for causing infections in hospital settings, have met their match in Mutacin 1140. "This antibiotic has the potential to treat such infections, which might otherwise lead to death of the patient," Hillman says. Approximately 100,000 patients died last year from infections they acquired during hospitalization.

The patented antibiotic peptide, also held under license from the University of Florida, is now in its preclinical phase of development and may obtain fast track status after application to the FDA as an investigational new drug. Zahradnik is optimistic that if all goes as planned, clinical trials will begin within a year from now.

"We plan to position it as a drug of last resort, and it can be used in hospital settings to treat infections not responsive to current antibiotics," Zahradnik says. "These multidrug resistance strains are of major concern in hospitals, but Mutacin is very effective in killing them. It has a unique mode of action compared with other antibiotics on the market so it fills a very important niche."

Replacement Therapy and Mutacin 1140 show great promise and are generating quite a bit of excitement. Following the completion of clinical trials, expected to take approximately four years, Replacement Therapy will hopefully receive approval from the U.S. Food and Drug Administration and become the first line of defense in tooth decay around the world.

That leaves just one problem: if a simple, painless topical treatment can offer kids a lifetime of protection, can we no longer threaten that eating too much candy will cause cavities?

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