



# The National Hair Journal Medical Section

PROMOTING COOPERATION BETWEEN THE ARTISTRY OF HAIR REPLACEMENT AND THE SCIENCE OF HAIR RESTORATION

## IN THE BEGINNING WAS THE FOLLICLE

### Does Hair Genesis Belong on Your Ark?

*A Google search for "hair loss treatments" delivers 45,100,100 hits. Narrow it down to "hair loss lotions" and you get 1,100,100 with names like Spironolactone, Phytologie Phytocyanine, Doo Gro Mega and Triple Gro Tea Tree Oil. You get the point. So how can a poor hair loss victim decide what works and what is simply a money pit? The answer is research. Not just anecdotal evidence and friendly testimonials, but serious studies validated by an independent third party. In this interview Geno Marcovici, PhD, Chief Scientific Officer at Advanced Restoration Technologies (ART) describes clinical studies that culminated in Hair Genesis, a botanically based hair care product that he claims is the only non-drug hair loss treatment tested and developed in collaboration with a university-based research team and the only non-drug hair loss treatment with a demonstrable dual mechanism of action. The Hair Genesis "Generation IV" regimen comprises oral softgels, a topical activator serum, and a special revitalizing shampoo.*

**NHJ:** Dr. Marcovici, you recently completed a hair regrowth study. Could you tell readers of The National Hair Journal in layman's language, what this all-natural product is, and how it can help their clients?

**Dr. M:** The formal name for the most common form of hair loss is "androgenetic alopecia." That's a big word, but in layman's terms "pattern hair loss" suffices. Let's put hair loss in context. In the United States, 40 million men are believed to be affected by pattern hair loss, and perhaps the more surprising statistic is that 20 million women in America are also affected. These statistics can be extrapolated out to much larger numbers when you consider the global



population. Hair loss has always been acutely distressing. Until recently, there hasn't really been much that's been effective in treating the disorder. Going back to ancient times in Egypt, historians have discovered that they used crocodile dung and all sorts of interesting substances that were purported to thicken the hair. And in the 19th Century, the term snake oil came into widespread use because they actually extracted oil from rattlesnakes and other reptiles as a hair growth accelerator. Today, we have more responsible choices... though a quick surf around the web could easily make you think otherwise.

**NHJ:** The FDA, has officially approved two hair growth drugs. Is that where the hair regrowth story stops?

**Dr. M:** There are actually three drugs that are presently indicated for pattern hair loss. The first is Minoxidil, which originally was a blood pressure medication. It is a topical product and is now trade named Rogaine. The second is Finasteride, which is an inhibitor of the Type 2 5-alpha-reductase enzyme, a key enzyme associated with androgen metabolism that in genetically susceptible individuals triggers the disorder. The third drug is a dual inhibitor of both Type 1 and Type 2 5-alpha-reductase and that is called Dutasteride. It is sold under various trade names including Avodart.

**NHJ:** Dutasteride has not received FDA clearance. Do you know their status?

**Dr. M:** I think it's in Phase 3 trials at this point, but

it's used off-label as a hair growth agonist.

**NHJ:** Where does Hair Genesis fit in?

**Dr. M:** Hair Genesis was originally developed in the mid-1990s and capitalizes on observations that we made that were serendipitous in that certain naturally derived substances, including saw palmetto extract and, specifically certain compounds within saw palmetto, beta-sitosterol, stigmasterol, campesterol etc. — other things like that had shown benefit in ameliorating the symptoms of a disease which is strikingly similar in its biochemical etiology to pattern hair loss. That disorder is BPH, or Benign Prostatic Hyperplasia. There are some well-controlled European trials that show that saw palmetto in high enough doses has a tendency to provide clinical benefits. So we began testing different compositions and formulations incorporating various strengths of saw palmetto and its glycoside beta-sitosterol. We came up with a formula that showed striking benefits in our clinic population. We went to market with that formula in the mid-1990s.

**NHJ:** Why did the market need another hair regrowth drug?

**Dr. M:** Hair Genesis is technically not a drug. It's a naturally derived composition. This is significant when you consider the pluses and minuses of the pharmaceutically-based hair growth drugs. The benefits of the FDA-approved drugs are self-evident; clinical evidence indicates that you can slow down, arrest, or in some cases reverse pattern hair loss. The downside however, is that both minoxidil and finasteride have been shown to present potentially significant negative side effects. If you read the side of the bottle, or if you look it up online, you'll find a lengthy list of negative side effects. So these are real caveats when you consider how badly you want to protect your hair. The nice thing about using naturally derived substances is that you have a much stronger safety profile. You don't see the sort of teratogenic effects, (i.e. feminizing birth defects), pulmonary edema, loss of libido, etc. that you do with the drug-based choices. Another thing we found particularly compelling was data from several investigators that suggested that carefully composed extracts of saw palmetto potentially offered between a 3-fold and 15-fold greater efficacy in inhibiting the pathogenic five alpha-reductase enzyme without triggering concomitant negative side effects. So we thought that this was a set of substances worth investigating. After several years of work we were able to demonstrate clinical benefits through two open-label studies before went to market. An "open-label" study, as you may know, is a study where the test material is dispensed with an open label meaning that the investigator and study subject are aware that the active material is being tested. This is in contrast to a placebo-controlled blind study where an inert material is dispensed to part of the study population while another group receives active treatment.

**NHJ:** What is the significance of the test subjects knowing they are using an active product? Is it to ensure compliance so they will stay with the program?

**Dr. M:** Not really. The benefit of an open-label study is that it constitutes what's called a proof of principle. If you see a demonstrable benefit under open-label conditions, then there's a reasonable probability that you'd achieve similar results randomizing the study subjects and going to a full double-blind trial. That's what we did in the late 1990s and 2000. The results of that placebo-controlled, IRB monitored, double-blind study still represent the only example of a non-drug-based hair-loss treatment to show clinical efficacy in pattern hair loss. That particular study is available for anyone to see on pubmed.com.

**NHJ:** People searching for hair loss remedies online will be presented with a list of products, some authentic, many unscrupulous. Why should they believe that Hair Genesis is different?

**Dr. M:** A valid question. Here's why. We were the first to market with a botanically based hair loss treatment in 1996. At the time there just wasn't anything else like Hair Genesis® out there. We opened the door to naturally derived substances in the hair loss treatment category. Early compositions of Hair Genesis incorporated minoxidil and some of our competitors took a page from our playbook. A couple of years later however, new data suggested that there were naturally occurring substances that could actually outperform Minoxidil plus saw palmetto. We used those compositions in the 2002 published IRB-monitored drug trial.

**NHJ:** What is the plant or tree from which saw palmetto is extracted?

**Dr. M:** The saw palmetto tree is like a weed version



Geno Marcovici, PhD

of a miniature palm, and it grows wild from the coast of North Carolina all the way down into Central America. It produces dark, pungent berries that have been used by Native Americans for a long time and purportedly offer all sorts of clinical benefits. Saw palmetto came into widespread use in Europe as a treatment for Benign Prostatic Hyperplasia (BPH). Investigators found that certain fatty acids and sterols in the berries were responsible for ameliorating the symptoms by blocking the 5-alpha-reductase enzyme. I was attending a conference in late 1993 and saw a poster discussing the benefit of using saw palmetto to treat BPH and in a kind of mini-epiphany I realized that BPH is precipitated by the same metabolic chain of events that causes pattern hair loss. It may be helpful to think about dihydrotestosterone, or DHT, as the gasoline that causes the inferno in hair loss that damages hair follicles. In the prostate gland, DHT is triggered by an enzyme called 5-alpha-reductase. 5-alpha-reductase is like the match that lights the fuse, okay? In the prostate DHT causes pathological growth that results in pain on urination and the potential for inflammation, infection, etc. In the hair follicle, the hormone causes the opposite effect in that the hair follicle involutes, or becomes miniaturized. So it occurred to me that if this stuff could block 5-alpha-reductase in the prostate, why couldn't we come up with a way to reformulate some of the key fatty and sterols in saw palmetto into a composition that would have benefit in the hair follicle.

**NHJ:** What happened next? Did you lock yourself away in a laboratory for six months, or form a new research team?

**Dr. M:** This was in the mid-1990s and we had a small laboratory and also a clinical facility. We also had some nice relationships with collaborative researchers, so we had access to the materials and tools we needed. Because we were a hair clinic, we had a built in population of highly motivated folks who were keen to help us find ways to help them stop losing their hair. From these people, we selected appropriate individuals - which for us meant relatively young to middle aged people in generally good health and also in the early stages of hair loss - and we put them on various test compositions to see what sort of response we would get. From that early work, we developed a set of formulas that became the product we market advanced versions of today. We originally called the line "ProAcTabs," but then we came up with a little bit better name, "Hair Genesis®."

**NHJ:** What is involved in setting up a clinical study?

**Dr. M:** To validate the clinical efficacy of Hair Genesis we needed to test the product under scientifically rigorous conditions. We enlisted a third-party clinical facility that was in the business of conducting independent tests like this one. The entire process was carefully monitored by an institutional review board, or IRB, which exists to ensure that everything is done according to highly stringent FDA regulations. The study was undertaken in 1999 and the data gathered between the end of '99 and early 2000. The results were clearly in favor of treatment. The placebo population continued to experience hair loss, while the treatment population showed a complete arresting of the progression of loss. Two out of three participants actually had thicker hair at the end of the trial. So that was a fairly impressive outcome.

**NHJ:** How do these results compare with other tested products?

**Dr. M:** Outside of the big drug companies, to my knowledge no one else is doing serious research in the category. If you go to Pubmed.com also known as Medline and type in "botanical" and "hair loss," only one research study comes up, and that is our clinical trial. If you think about it, it's astounding that nobody else has thought it important to validate their products using the same high level of scientific scrutiny.

**NHJ:** How do your results compare with Rogaine?

**Dr. M:** We compare favorably with finasteride where two out of three patients showed a response. Where I think we have potentially an inside track is the fact that our product line doesn't suffer from the negative caveats that finasteride, dutasteride, and minoxidil have.

**NHJ:** What is Advanced Restoration Technologies engaged in right now?

**Dr. M:** We realized that pattern hair loss is not simply the result of 5 alpha reductase mediated dihydrotestosterone damaging the follicle, even though most of our competitors have been chasing that metabolism forever. AGA is known as a complex trait disorder. This means that there are numerous factors, genetic, biochemical, epigenetic and environmental that are responsible for triggering the onset and progression of the disease. One can appreciate

the variable factors that influence AGA by observing how many ways people can suffer from the disease. Some people lose hair in front, others only in back, while still others lose hair across the entire front and top of the scalp. So clearly it's not simply about one factor, i.e. dihydrotestosterone. And so what we set out to do was to say, "Okay, we need a new hypothesis. If there are other things going on, wouldn't you get a better clinical outcome if you could identify one or more of these other causative factors and then target those contributing factors while simultaneously hitting dihydrotestosterone and 5-alpha-reductase?" So that was our overarching hypothesis. We were fortunate to have sharp collaborators at the University of Albany and elsewhere who helped us think creatively about this part of the problem for a couple of years. Ultimately, we identified several inflammation-related events in the hair follicle that seemed to be really important. From that, we went on to identify a series of genetic markers that seemed relevant in the setting of pattern hair loss. We tested our theory in a set of basic science experiments, for example using a well-respected analog for hair follicle biodynamics called HaCaT cells. These cells are a type of keratinocyte found in the skin and, specifically the hair follicle. Once we had identified the important gene markers that were associated with inflammation in the hair follicle, we designed a set of experiments where we actually went in and used a type of irritant, called lipopolysaccharide, or LPS. Then we applied a formulation representative of our latest generation of product and we were able to show a statistically significant reduction in the level of key markers of inflammation. Given what we know about inflammation and hair loss, from a basic science standpoint, that's a reasonable proof of principle that you have a new mechanism of action as well as a new way to treat the problem. So next, and to protect our hard won efforts, we took the extra step of going back to our IP council and filed a USPTO application to protect the novelty of what we'd come up with. We then submitted the results of our work to a well-respected journal, and that's the link we sent to The National Hair Journal.

**Dr. M:** These new data, coupled with our previous clinical research, gave us the impetus to create our Generation 4 Hair Genesis product formulations which are just now hitting the market.

**NHJ:** Do the medical and research communities, accept your results and your conclusions?

**Dr. M:** Yes.

**NHJ:** What would it take to go to the next step and conduct a study that would satisfy the Federal Drug Administration?

**Dr. M:** If we were interested in characterizing Hair Genesis as a drug, there's a research regimen protocol we'd have to follow. However, our preference is to remain an all-natural or a cosmetic product. We're operating under the auspices of the 1993 DSHAE (Dietary Supplement Health and Education Act) rule. So though we're fairly confident that the product does even more good in the hair follicle than we describe, we prefer to under promise and over deliver.

**NHJ:** What new research is planned?

**Dr. M:** We'd like to do a multi-arm study where we might have gender-specific populations. We might even test Hair Genesis against some of the well-known hair treatment drugs.

**NHJ:** Who could benefit from Hair Genesis? Is it suitable for both men and women?

**Dr. M:** Yes, the product works equally well in women and men. However, the regimen is most beneficial when it is begun early in the disease process. As an analogy, our viewpoint is that a parachute works best before you hit the ground. For people who have lost most or all of their hair, laser therapy's not going to do it, and Hair Genesis is probably not going to do it either. The hair follicle at some point loses the ability to hear a signal or to receive a signal to return to healthy vigorous growth. So our suggestion is that it's better to start any treatment sooner rather than later and we find our clients are most happy when they use Hair Genesis as a hair maintenance program rather than trying to make up for lost ground.

**NHJ:** Does Hair Genesis arrest hair loss or promote new hair growth?

**Dr. M:** Hair Genesis inhibits the factors that are known to trigger hair loss. So if you can block 5-alpha-reductase, and if you can reduce the pathologic inflammation of the hair follicle, then you can, from an anatomical and physiological standpoint, preserve those structures so that they can produce a more robust product, which is the hair shaft. othing grows new hair. You die with the same number of hair follicles that you were born with. Pattern hair loss is miniaturization of the structures and sub-compartments of the hair follicle. But if you can get ten hairs that are twice as thick, it's as good as having twenty hairs.

**NHJ:** Final question; how did you get into the thinning-hair field?

**Dr. M:** My mother was a manicurist for 45 years, my dad a hairstylist from Europe. So I started out with perm solution in my blood. (Laughs) I'm married to a hair scientist. I guess you could say I'm continuing the family business!