You spent nine years doing basic research aimed at understanding skin disease (including aging) and barrier function. What did you find?

**Dr. Thornfeldt:** We identified two critical factors that activate everything else we see in skin aging. Number one is a disrupted stratum corneum barrier. Second is uncontrolled, chronic inflammation in the epidermis and basement membrane zone. We found that epidermal function and inflammation are regulated by that integrity of the stratum corneum. Any stratum corneum disruption induces inflammation.

We found that there are seven pathways of inflammation that occur in the skin that, coupled with disrupted stratum corneum, produce the changes that we see as skin aging. All the changes we see with skin aging can be pointed back to these seven pathways of inflammation. Five of those pathways are the direct result of disruption of the stratum corneum barrier in and of itself. Then the inflammatory processes that were initially to heal and repair go awry and result in what we see as diseased skin and damaged skin including aged skin.

We also found there are five barrier repair pathways. To produce rejuvenation of the skin, it is critical to repair the barrier. The initial process for repair is upregulation of synthesis of the three key skin barrier lipids: cholesterol, 11 ceramides, and free fatty acids, of which 50 percent must be linoleic acid. We know that a specific cholesterol-dominant ratio is the critical factor for optimum barrier function. There was no clinical difference between 0.6-5.4% by weight.

The problem is that other therapies only work on a portion of these pathways. But of those seven inflammatory pathways, only two are affected by antioxidants. Nobody doubts that antioxidants have some benefit, but I’ve never had a patient come in to me and say, “Doctor, I would like to get two sevenths improved”? In other words, “I want complete clearance of two of the pathways, but I don’t want you to mess with the other pathways.” A critical aspect for disease control is that you have all these seven pathways involved thus need to be modulated.

Your product development ultimately focused on botanicals. Why? What did you learn?

**Dr. Thornfeldt:** There was no way we could formulate with enough synthetic agents to block all seven inflammatory pathways and up regulate all five barrier repair pathways.

It’s also important to realize that there’s a continual process of insult. Consider the tyrosinase inhibitors for hyperpigmentation. They do have benefit, but there is a rapid rebound and a high rate of recurrence. The high incidence of post inflammatory hyperpigmentation is all because intended treatments damage the barrier more. We found that just turning off that chronic inflammation in the skin removed 37 percent of the hyperpigmentation within 12 weeks.

This whole aspect of the barrier has really been under-investigated and under controlled with most therapies. I knew that big pharma would have no interest in that, so we went ahead.

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and started Episciences. The foundation of Epionce is that it’s the first company that repairs and optimizes structure and function of the stratum corneum. It was the first company to have products that modulate all seven inflammatory pathways and five barrier repair pathways of aberrant cells in the stratum corneum, epidermis and basement membrane zone.

There were no synthetics that would produce these functionalities, so we went to the botanical arena because there exist many biologically active molecules that remain in stable, functioning activity that can be formulated together. It’s just not the presence of a botanical; The issue is whether you can deliver enough of that secondary metabolite—in other words: the active ingredient within the botanical extract at the therapeutic concentration to the specific cell or structure.

What are challenges of formulating with botanicals?

Dr. Thornfeld: The challenge is whether you have enough potency and concentration of secondary metabolites in the extracts that will remain stable in the formulations that you make. To prove that, not only did we have to do various concentration and formulation bases tracking these different herbal ingredients, we needed to know exactly what active compounds were in each one of the herbal extracts. Thus, controlling consistent function is extremely important with herbal products.

A critical aspect for herbs is the extraction methodology, but that herbal product that you extract from is subjected to a whole variety of environmental changes that will affect the ratio of those active ingredients. The secondary metabolites are used primarily for protection, for storage, and to help the plant maintain homeostasis. They are subject to environmental and process variations. Consequently, all of the other methodologies from harvesting and processing play a big role. We developed proprietary ways to purify and stabilize our herbs so that we know what those active ingredients are. We know the concentration. We know what concentration can be utilized by the cell, and how to deliver it to that cell.

Now, the only way you can prove that that actually works is then taking that final formulation and doing prospective, controlled, double blinded clinical trials against placebo and then against a known active agent, such as an OTC drug or a prescription drug. That’s why we do all these trials. We just finished our twenty-fifth of these clinical trials. We do those trials because we want to prove that, in fact, our theories actually work.

Another reason we use botanicals relates to my training at UC San Diego under Dick Stoughton that really characterized the role of tachyphylaxis. Dr. Stoughton found that if you could have two inhibitors of each one of the steps in the pathophysiologic process, then the chance of developing tachyphylaxis dropped by over 90 percent. We know that there’s a dynamic world out there, and you’ll be using these skincare products for a long period of time. We needed to make sure that our botanical extracts, the combination of those botanical extracts manipulated every single one of those seven inflammatory pathways and all five barrier repair pathways with at least two active ingredients. Then that allows you to continue to have functionality of the product and safety over the long period of time.