



Sept 2008: Interview with Dr. Michael Zemel on Innutria™

How did Innutria get started? What gave you a light bulb moment?

We started Innutria as a result of the experience I gained working with dairy and weight loss. My laboratory is the laboratory that developed the concepts that there were components of milk that would promote healthy weight management and augment the beneficial effects of calorie restriction on weight loss. As we went through that process, I learned a lot, and I began to realize that milk is not the only magic food. We discovered the milk weight loss connection through a series of basic science steps which were built around understanding how fat cells work. The light bulb moment was when I realized that I could export these concepts that I could use the same science as a discovery tool to find similar activity in other foods and other nutrients, and so we developed a screening system using human fat cells essentially as a sensor and began looking at other activity not randomly in a direct way in places where I thought it ought to be and from that we built up the Innutria concept.

Tell me a little about the research throughout the stages of the product development?

Please remember that Innutria is first of what we consider to be a family of products. I have no intention for Nutraceutical Discoveries, Inc. (NDI) to be a one hit wonder. This is an ongoing process. We hope to have a family of Innutria products oriented at different health based markets, men's health, women's health, metabolic health, weight loss, active living, etc. With that as a backdrop I was chasing after one component for what was to become the first component of Innutria and I already developed some theories about it. We tested those theories, human cells first, fat cells and muscle cells because we had proposed that it would mediate a switch in how energy was used, and essentially move energy and calories away from fat cells into muscle cells; instead of extra energy or calories being stored in fat, they would be used in muscle burned to support new protein synthesis. We tested these concepts out in cells and it was proved to be correct. We refined them, of course, and then tested them on animals and the concept held. We then took it to clinical trial to confirm that it would work in people; each of these steps is necessary because what happens in cells is good enough to make you feel good but may not prove enough to be true in mice. And if it's true in mice you've got a better shot of it being true in people but you still don't know. You've got to have clinical confirmation. Our clinical confirmation in this case was better than we could have expected. It actually went better in people and so that became the corner stone of what was to become Innutria.

How exactly was it tested in people?

There were several versions of clinical trials. In one version, we give people Innutria™ or a placebo and put them on a diet. So everyone gets to lose weight but we look for the ability of Innutria™ to augment the weight loss over the placebo and not just weight but fat loss. We also look for specific changes in what we're terming metabolic health, inflammatory stress and oxidative stress. In another implementation, we don't put people on a diet we simply look for the ability of Innutria™ to promote fat burner and the ability of Innutria™ to promote metabolic health. So we've done all of those things. We have added, since we started the company, we've added to what things go into Innutria™. We've sharpened it a little bit, by adding an additional compound. Which really turbo charges the affects and this additional compound really accelerates the ability of Innutria™ to increase fat loss.

How many versions did you go through to get to the point you are at now?

Goodness, this is an interactive process. We play a little bit in the laboratory. I would say 4 or 5. But as I say we're not done. Now, I think we are done with what we have. I think this is the best that this version can be. We're not going to come out next year and be like the laundry detergent, the new and improved instead we'll be adding new functionality. We are hoping to have a product that focuses on pediatric health. We're especially concerned with what the American Academy of Pediatrics came out last month with a list of policies recommending the use of low fat and fat free foods, milks for children as young as 1 year of age, approving the use of statins, cholesterol lowering drugs for children as young as 8 years of age. I'm bothered by this and I think that if NDI can do something to promote pediatric health rather than putting children on drugs, I think we will have made a big contribution. I think Innutria™ as it stands right now can do that but I think we could do it better. I think with a little more R&D we will have a better formulation...one that is better suited for children.

Is there any chance of Innutria™ being used in synthetic infant formulas?

Probably not. The goal of a formula an instant formula is to become as close to human milk as possible and then to add functionality where functionality is warranted. For example, the first major change in infant formulas is for a long time was the addition of DHA and that started with one company and now they all have it. DHA makes sense; at one level it's an additive but at another level DHA appears in breast milk, just a varied degree depending on what mom ate. And we know that infants who get more DHA do better in a variety of indices and so it made sense. You don't mess, in my opinion, with infant development and I come from a perspective of wanting as many infants as possible to be on breast milk so I'm not eager to do anything that adds or subtracts from what's in human milk.

Where would be the best age to start with?

That is a very interesting question and I actually do not have an answer. If you had asked me this question a year ago I would have said preteen, but now that AAP is suggesting stats as low as 8 years of age and certainly we recognize the impact of the obesity epidemic in primary school children....again I don't think you mess with what works. I don't think you want

to be targeting kids who are basically lean and healthy, but I would say certainly primary aged children. And the nice thing here is there is nothing in Innutria™ that is not natural, that is not already present in the diet. We're optimizing how much is in the diet but we are doing nothing that could threaten the child's health (or an adult's health for that matter). Personally, I would like to put it into our dog and cat's food as well, as any veterinarian will tell you that our obesity epidemic has now spread to our pets as well!

What part of the obesity epidemic or how much does that play in coming up with Innutria™?

I have been consumed with the obesity epidemic. My goal is to help ameliorate the obesity epidemic and not just to make us all thin. Look, let's be realistic there is nobody in America who doesn't get that we could get thin if we ate less and exercised more. There is a gap between what we know and what we do. We have good intentions and life gets in the way. We want to use the gym but we got to pick the kids up at school and take them to practice or whatever. You could have a million versions of that excuse for any of us. Life is more complicated than it used to be and we have more things that help us do our work. That's the bad news. The good news is that it's really a small imbalance between what we eat and what we do that causes the obesity. The average American adult gains 1 to 3 pounds per year. It's not even linear, it's not month to month, you gain weight just when you think you would, around the holiday and you lose some and you gain some and then by the end of the year you're between 1 and 3 pounds heavier. Average is a little less than 2 pounds a year. You don't even notice it until you hit that milestone birthday and you put on the old jeans and there's about a 2 inch gap between the buckle and the snap and so then you start feeling bad, but in fact we get here in small increments...just a few calories at a time. What makes that good news for a company like NDI is it just takes a small nudge in the other direction to succeed, and Innutria™ amplifies the effects of that small nudge. At the same time I want to do more than just fight the obesity epidemic because I'm under no illusion that everybody who consumes Innutria™ is going to return to their ideal body weight. Instead I want to be able to support metabolic health, the consequences of obesity. I want to look at somebody who asks the question can I be a little overweight and healthy, can I be fit *and* fat instead of fit *or* fat. I want to be able to look at them and say yes and what we could do is use something that will help protect you against some of the consequences, we still want you to lose weight but we want to protect you against the consequences of being overweight, we want to do both. Now the cool thing about Innutria™ is it's a multifunctional compound...it sounds almost too good to be true. If somebody tried to sell me something like this I'd say it was too good to be true but we have data and I believe data! What I mean by that is it also services people who are not fat because it helps promote fat burning. It provides a nice augmentation of an already healthy lifestyle. Somebody who's going to the gym or running and simply wanting to be better...well, burning fat helps you be better.

Describe what metabolic health and cardiovascular health actually are.

Metabolic health is a term that we have used as shorthand and I understand that it's not yet in the American Lexicon. It kind of sounds good but what does it mean? I use that term as

shorthand for two other terms which are also not yet in the American Lexicon: inflammatory stress and oxidative stress. Now the latter of those two people kind of get; they may not get the term oxidative stress but everybody knows that we're supposed to be taking antioxidants. What causes disease? What causes obesity to make you sick? Well two major causes of obesity-induced disease oxidative stress and inflammatory stress. The oxidative stress really increases your risk diabetes while the inflammatory stress promotes cardiovascular disease, so we would like to suppress the root causes of these metabolic diseases. You may not realize but the medical community has redefined cardiovascular disease as a sub clinical inflammatory issue. It is the small inflammations that cause the problems, that cause atherosclerotic plaques to build up, that cause blockages that cause strokes and heart attacks. What we would like to do is reduce that inflammation. We'd like to cut it off at the source and your fat cells are one of the key sources of this inflammation and our key ingredients of Innutria™ do a great job of suppressing that.

What causes inflammatory stress?

Well lots of things cause inflammatory stress but what we focus on is that when a fat cell gets bigger, it changes what it does. So everybody thinks that a fat cell is just a bag of fat and so we have a lot of bags of fat in our body; not so!. Fat cells are very active endocrine organs secreting lots of hormones. The problem is the hormones that they secrete change as fat cells go from small to big and as they get bigger they get nastier and part of that nastiness is they secrete some compounds that are inflammatory and then they secrete some other compounds that essentially invite some other cells to live with them in fat tissue and those other cells are inflammatory cells and that combination is just dynamic in spitting out inflammatory compounds. On the oxidative stress side people are used to the concept of antioxidant, they get that antioxidants are good for you. Innutria™ has no antioxidants in it, at the present. Why? Well because half of the folks already are getting enough antioxidants and we don't want to gratuitously any, that is not our purpose. Everything we put it does and will have function plus too much antioxidants can be harmful. We know this from clinical trials. What people may not realize is several of the antioxidants that people like to take as supplements can also serve as pro-oxidants. So what's Innutria™ got to do with oxidative stress? Antioxidants help essentially scavenge oxidative stress. In contrast, Innutria™ helps suppress with production of oxidants. From my perspective we have tried to design Innutria™ to work with your body to maintain a state of health, optimize your health. It's not a cure for any diseases.

Tell me about what types of products or foods Innutria™ is best suited for.

Right now, Innutria™ is best suited for multiple kinds of foods. Our first launch is with Attitude Drinks and milk is a great vehicle for Innutria™. Because milk, skim milk, is low in calories but high in nutrients. It's the perfect combination for somebody on a diet. We add to that the functionality of Innutria™ to enhance the weight loss and fat burning as well as the metabolic health; you really have an ideal situation. However, we can put Innutria™ in waters, teas, other beverages; we can incorporate it into foods, structure foods, and solid foods. Now there's a limit to what makes sense. I'm not going to suggest that we should fortify bacon with

Innutria™. I think we need to put Innutria™ into the context of a healthy lifestyle. I don't want anyone to get the notion that we think that adding Innutria™ to a nice rich bowl of super premium ice cream will somehow neutralize the calories. It won't happen. The number of inappropriate vehicles for Innutria™ is much smaller than the number of appropriate vehicles. There are many foods that may not be currently thought of as being "functional" which in fact could be.

What would be an example of some of those?

Well let's think about some of the foods that are already on the market. Oats, oatmeal, oatmeal has functionality, but what else has functionality? There are other high fiber, low energy food products that have protein to them, beans for example, that's one of many examples.

Innutria™ is a functional ingredient, that's how foods become functional. It could also be in a clever way paired with other functional ingredients.

Tell me about the sound science and the validation and proven statements that have proven a valid supplement.

What makes this a valid supplement is the following; none of these steps individually will suffice. We have mechanisms, we know how it works. That's from cellular, molecular, mechanistic studies. Would that be enough for you to take something? No, it wouldn't be enough for me to take something. We then have proven these concepts by manipulating mice. They are good mice, they are humanized mice. So far I haven't seen anything that's worked in these mice and hasn't worked in people. That just tells you that I have a lot of faith in these mice. Not that I'm willing to go forward and treat people with something or give people something that hasn't been tested. We have then tested each one of these claims in people...there is a science behind each one of these claims. So I have data to show that Innutria™ will reduce inflammatory stress, it will significantly reduce inflammatory stress. It will significantly reduce the production of reactive oxidative stress. It will significantly enhance fat burning, when you compare our fat burning effects and the effects of the other compounds that are frequently used in nutraceuticals, like green tea or extracts of green tea or CLA, is a common one, we are easily twice as effective. We can augment the effects of energy restriction by 50% – 70%. That's huge! So, if your efforts were going to cause you to lose 10 pounds with Innutria™ those same efforts could cause you to lose 15 – 17 ½ pounds. And we've got the hard data to prove it.

If someone were to say prove it, show me your data, how would you explain that or tell me a little bit about the data itself.

What people considered proof are randomized clinical trials and that is what we have done. We have taken our data and applied our compound in randomized clinical trials. We take the target population, we recruit people and they get randomized into an active treated group or a control group which gets a placebo or some of our data like the metabolic health data. Each person actually gets both we cross them over in the fat burning part we don't do that.

Are there other ways that are used other than random clinical trials?

Anything else would be supportive but not definitive.

Anything else you want to say?

We want to be the good guys. We aim to be the good guys. We want to be the trusted source for nutraceuticals, the food industry, those that we discover, those that we mix, and those that we help identify as being useful. We are not going to push anybody into to utilize something that we are not absolutely certain about. There are a lot of products out there that are lining the aisles making outlandish claims. We will avoid that like the plague. We don't want to be a part of that. I have no doubt that people are making money doing it I guess they wouldn't do it if it didn't bring them a profit. We just want no part of it. I am a university professor as well as a principal in NDI... we are maintaining and will continue to maintain our scientific integrity. We want to hold ourselves out as the credible source.