

## Commentary

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Nineteen Ninety-One. Seems like a life-time ago. Grunge, the Gulf War, Nirvana, Twin Peaks. A young very bright clinical fellow, Dr. Rob Lane, walks into my office and says “we should study the intrauterine growth restricted (IUGR) offspring after birth in our IUGR rat model.” I asked “why in the world would we want to do that?”. At the time, we were focused on the impact that uteroplacental insufficiency had on glucose transport in the fetus. I had a grant and was feeling pretty good. Rob replied, “haven’t you heard of the Barker hypothesis?” I answered, “Barker who?” Rob proceeded to enlighten me. And thus, began a new journey. Fast forward 5 years later. My family and I moved to Philadelphia. The University of Pennsylvania had one of the preeminent Diabetes Research Centers. This was going to be great. I met with two senior investigators in the field, one a  $\beta$ -cell biologist, and the other, a researcher in the field of glucose transport. When I explained the premise behind fetal programming of adult disease to these world-renowned scientists, I was met with intense skepticism, and in fact, some derision. However, I was not to be deterred. I persisted. At every research conference, every mentoring meeting, even in the hallways, I took the opportunity to discuss the Barker hypothesis. People began to avoid me “Uh oh, here comes Becky Simmons. Hide. She is going to badger us about FOAD (Fetal Origins of Adult Disease).” I submitted countless grants. Rejection is hard. Nonetheless, I persisted. My husband wondered why I kept banging my head against the wall. However, he had very good advice and suggested framing the question in a way that scientists (especially evolutionary biologists) in the “adult research world” would understand. He taught me how to write a better grant and to make a better argument. He edited and re-edited grant after grant after grant. One finally hit. Without his support, I would not be where I am today.

A research career zigzags. Success, failure, failure, retooling, success, etc. I took my cues from David Barker. Never give up. Evolve. Keep your eyes on the horizon. With that in mind, we pursued the idea that altered mitochondria function in the growth restricted-fetus played a fundamental role in  $\beta$ -cell dysfunction leading to the later development of diabetes. A few years later, the field of epigenetics was exploding. Another brilliant young scientist, Dr. Rob Nicholls and I were having lunch, with a lot of beer. Beer allows you to free-associate. We could call it Beer Origins of Research Grants (BORG). I suggested that he assess mitochondria function in his animal model of Prader Willi. He suggested that I examine epigenetic modifications in our animal model. “Why would I do that?” I asked. “Duh,” he answered. So, once again we changed directions. Who knows where we will go next? This is what makes science so fun, and so challenging. What is just over the horizon?

A research career does not flourish in isolation. To borrow a phrase from Hillary Clinton, “it takes a village.” The foundation of that village are the students and trainees. They challenge us to think outside the box. They bring energy and enthusiasm, and occasionally, food to lab meetings. I have mentored and trained over 100 students, postdoctoral and clinical fellows over the years and each one of them has contributed to the success of our research program. Without them, I would not be where I am today.

The pillars of the village are our colleagues and collaborators. Team science is critically important and outstanding research does not occur in a vacuum. With the explosion of techniques and big data and decreasing grant resources, it becomes necessary to collaborate. Colleagues also provide shoulders to cry on, sounding boards to bounce crazy ideas off of, and most importantly, friendship. Without them, I would not be where I am today. Without each other, none of us would be where we are today.

Another pillar of our research village is our funding agencies. I know that sounds odd. We curse those summary sheets, complain about lack of dollars, wonder why it takes YEARS to get a grant. Yet, the NIH, the March of Dimes, and the American Diabetes Association have all funded my crazy ideas and the crazy ideas of my friends and colleagues. They too, through RFAs, and other mechanisms, have allowed us to think outside the box. At least sometimes. They believed in the Barker hypothesis when the senior scientists at my institution did not.

The Barker hypothesis has evolved and has been renamed. Yet the concepts persist and drive critically important research. In these troubled times across the world when the health and well-being of mothers and children seem to not matter, the scientists who commit themselves to this research question have persisted and will continue to pursue their ideals. It is our mission to train the next generation of scientists to carry that torch.