By Alissa Poh

A DISCUSSION WITH

PETER BAUMANN

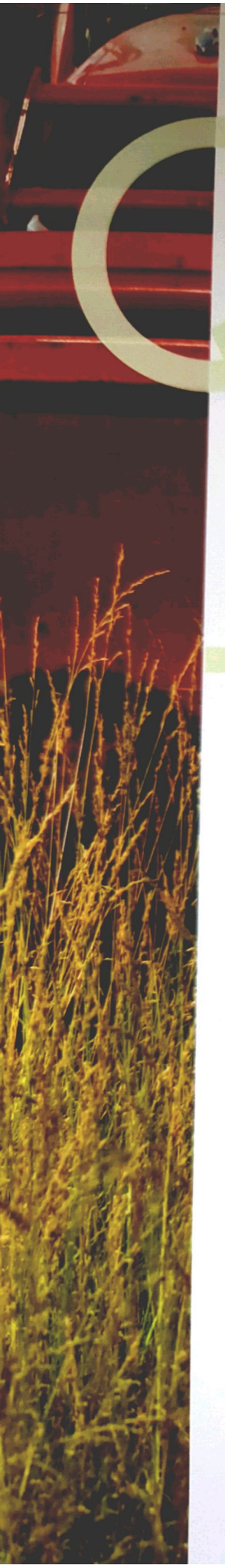
Investigator Peter Baumann, PhD, fondly recalls portraying the lovelorn poet Eugene Marchbanks in the George Bernard Shaw play *Candida* during high school. "Being the same age as my character made it even more interesting," says Baumann, who grew up in Germany. He even considered a stage career, changing his mind after learning from professionals that acting was much more fun when it wasn't a job.

He decided instead to indulge his passion for creativity through science. "I wanted work that would leave me with a sense of accomplishment," he says, "so I settled on exploring the interface between biology and chemistry." And Baumann hasn't looked back. After defining the protein Rad51's role in DNA repair, his postdoctoral studies shifted to chromosome ends. Pot1, the protein Baumann discovered to be vital for protecting telomeres, jump-started his career and landed him his first faculty position at the Stowers Institute in 2002.

Where Baumann's innate curiosity leads, animals inevitably follow. When he was eight and trawling the Danube for larvae one afternoon, he rescued two orphaned mallard ducklings. They domesticated well, quickly wising up to the fact that young Baumann armed with a shovel in the garden meant a windfall of worms. "If I paused too long at digging, they'd nip at my trousers," he says. "Ducks are quite capable of learning—at least in exploiting food from humans." He's had opportunities aplenty to make other anecdotal observations about poultry. A handful of backyard tomato plants became, in Baumann and his wife, Diana's, hands, five acres of suburban homesteading, which more recently burgeoned into forty acres of sustainable farming—with chickens and ducks galore—southeast of Missouri's Smithville Lake.

Then there are the whiptail lizards Baumann's investigating. He's long been intrigued by the molecular basis of parthenogenesis, or asexual reproduction among certain all-female reptile populations. "It's a stretch, studying this alongside telomeres and RNA processing," he admits. "But to me, it's all chromosome biology."

For his prowess in both fields, Baumann was appointed one of just twenty seven new Howard Hughes Medical Institute (HHMI) investigators—from more than 1,200 applicants—in May 2013.



WHAT FUELS YOUR CURIOSITY, AND IS THERE A METHOD TO YOUR MADNESS OF SIMULTANEOUSLY TACKLING MULTIPLE SCIENTIFIC MYSTERIES?

I've always been more interested in testing the boundaries of what we know and never got out of the "Why?" phase all kids go through. But I don't find multitasking productive; it's better to be really focused for a limited time—for instance, spending several hours thinking only about telomere biology. That's when the best ideas come to me.

I also enjoy letting my mind run along a specific topic while something else is going on; I can watch a movie and not even remember that I did. Some research seminars are harder to get into and I'm inclined to give up trying if, a third of the way through, I still haven't grasped the main point. But I walk away thinking the time was incredibly productive anyway because I've come up with new ideas.

WHY HAVE WE MADE SO LITTLE HEADWAY IN THE HUNT FOR TELOMERASE INHIBITORS THAT MIGHT PROVE THERAPEUTIC IN CANCER AND AGING-RELATED DISORDERS?

In my opinion, by trying to measure telomerase activity we have been barking up the wrong tree. Less effort has been put into cell-based assays, because it's much harder. Over forty eight hours, the enzyme lengthens a few telomeres by just one to two percent resulting in a tiny signal-to-noise ratio. My ideal assay, which we're working on at Stowers, would measure the effect on telomere length, not telomerase activity.

We can keep looking for something that jams telomerase's active site, but the history of HIV research should remind us that it's difficult to suppress a reverse transcriptase in a cellular context without multiple side effects. That's why I'm more interested in the complex machinery required to make a functional ribonucleoprotein (RNP), so we might have other avenues to exploit in preventing telomerase from ever becoming active.

WHAT MADE YOU DECIDE TO TAKE A SHOT THIS YEAR AT FULL HHMI INVESTIGATOR STATUS?

It's really through my HHMI Early Career Scientist appointment [awarded in 2008] that I've been able to study parthenogenesis in whiptail lizards. Having since published in this field, I realized that I could no longer regard my lizards as a side project. But neither did I want to abandon telomere research. Knowing HHMI's nonconservative nature in selecting investigators, I decided to stick my neck out and show them who I really am: someone investigating RNA processing in telomerase biogenesis, who would also like to bring this other field, still mostly unexplored, to the same level of mechanistic detail. Apparently, this charmed the review committee.

From front to back: Chloe, Peter Baumann, PhD, and Dakota

SPEAKING OF PARTHENOGENESIS, WHAT GOT YOU HOOKED IN THE FIRST PLACE?

The notion of long-term sperm storage, which was postulated when zoos housing only females of reptiles like Komodo dragons and Burmese pythons found themselves dealing, inexplicably, with offspring. Perhaps, like some amphibians, there were compartments in these female reptiles where sperm could hang out at the right ambient temperature. If so, did the females release some factor to help keep the sperm viable, and could one adapt that for, say, overcoming the loss of viability associated with freezing sperm?

In retrospect, we were probably looking parthenogenesis dead in the eye, but it was the nineties and techniques like genotyping or deep sequencing had yet to emerge. Then Diana and I had dinner with Bill Neaves [president emeritus of the Stowers Institute] and his wife and learned about his seminal studies, back in the sixties, identifying the sexual hybridization that resulted in all-female whiptail lizards.

My question to Bill was, "So what happens to meiosis?" [Meiosis halves the number of chromosomes in sperm and eggs in preparation for fertilization.] And he answered, "We still don't know." I was sure that somebody had to have figured out an answer. But after first discovering that PubMed is not a good source for papers on herpetology, then spending a long time in the library, I concluded that Bill was right. That's how I got started. It's a fascinating difference that makes reptiles stand out among vertebrates: They're the only group that can be truly independent of males.

SO DINOSAURS REPRODUCED ASEXUALLY?

Michael Crichton employed the idea in *Jurassic Park*, a story that involved a hefty dose of artistic license. But while I am not aware of any scientific evidence in support of unisexual dinosaurs, I don't know of any data that rules out such a scenario either. It's an intriguing possibility, though, that there may have been periods in evolution's history where parthenogenesis played a more pivotal role than we currently assume.

AS YOU'VE SAID, THIS IS ALL A LARGELY UNCHARTED AREA OF BIOLOGY WHICH YOU'LL KEEP EXPLORING, MAINLY THROUGH YOUR HHMI RESOURCES.

Absolutely. To me, it's forensics – using comparative genomics to piece together a story from ancient records to current vertebrates. During hybridization, it's not that changes accumulate at a constant velocity over the next ten million years. There are very rapid changes initially, providing the adaptations necessary for a particular hybrid to work. There's scant research on this, but now that we have the tools to change an organism's ploidy and analyze the immediate consequences and effects over a few generations, it's an exciting endeavor.

LATELY, SCIENTIFIC MISCONDUCT HAS BEEN INCREASINGLY ON PEOPLE'S RADAR. HOW DO YOU PERSONALLY DEFINE SCIENTIFIC INTEGRITY?

I grew up in a scientific culture that emphasized getting it right, rather than being first. That's no longer the norm, which I think is terrible. With every paper published, countless hours of people's lives go into trying to repeat that work and build on it. Too often, they can't. Instead of providing an integrity compass and encouraging creativity, today's investigators have to publish, almost recklessly, just to hang on to their funding.

WHAT'S ONE PIECE OF ADVICE YOU'D GIVE TO THOSE JUST STARTING OUT IN ACADEMIC SCIENCE?

Don't burn bridges. You've heard of Sayre's law: "Academic politics are so vicious because the stakes are so low." We get into squabbles and break off contact with each other over really trivial things. The longer I am in science, the more I realize how this behavior does everyone involved a great disservice.

IF YOU HAD A TIME MACHINE, WHERE MIGHT YOU GO AND WHY?

If I could go to any point in time, I'd like to go all the way back to the origin of life, to see the earliest hints of what we now consider a cell. It's a fascinating topic, given all the initial obstacles that had to be overcome to make a functional organism. Hopefully, conditions wouldn't be such that I'd burn up immediately upon arrival.