PROTEINS AND TIGERS AND HORMONES! OH, MY!

by VICKY CERINO

WHILE STUDYING EARLY PREGNANCY LOSS, A UNMC SCIENTIST DISCOVERS A BETTER WAY TO PURIFY PROTEINS

To researchers, scientific discoveries are like dangling fresh meat in front of tigers. They are impossible to ignore.

Such was the case for Elliott Bedows, Ph.D., and Jason Wilken, Ph.D., whose discovery significantly changed the course of a research project and may ultimately benefit humans and endangered tigers. It also may impact a $36 billion-a-year industry.

The project: Advance reproductive biology in humans.

The problem: Discover the cause of pregnancy loss within the first three weeks of conception.

The approach: Compare the structure-function relationships of human chorionic gonadotropin (hCG), a hormone made in response to human pregnancy, to mCG, the parallel hormone of the Macaque monkey.

Conventional wisdom said the two hormones had identical physiological functions.

But, Drs. Bedows and Wilken, a graduate student at the time and now a postdoctoral fellow at Yale University School of Medicine, found a difference that challenged scientific literature.

To prove their findings, they ran their arduous experiments again and again.

"We wanted to find the difference, so we built new, but related proteins to study," said Dr. Bedows, associate professor, UNMC School of Allied Health Professions.

"We had to figure out how to purify all of these proteins – called recombinant proteins. We developed a technique that's much faster, cheaper and safer than anything that existed."

By safer, Dr. Bedows was referring to the toxic chemicals that are often used in basic cell biology research. Using these chemicals drives up the cost of the research and ultimately the cost of drug development.

Recombinant proteins are natural proteins engineered in a different cell system to replicate large quantities of proteins for use in commercial industry, drug development, research, and in diagnostic applications. But before recombinant proteins are useful, they must be purified.

The technique did more than purify the targeted protein; it purified every protein they tested with the same general shape.

"It's a unique concept because most purification schemes work on charge or on an amino acid sequence, or some other basic chemical aspect. Our technique targets the shape of a molecule, which is why it's such a novel approach," Dr. Bedows said.

Although some of the findings were published in the journal "Biochemistry" between 2004 and 2007, there is more to the story.

The technology ultimately caught the attention of UNeMed, the technology transfer organization for UNMC. The technology was so compelling that it was identified as having commercial potential. It is now being further developed, with several patents pending.

The possibilities for Dr. Bedows' new technique are vast in the recombinant protein purification world, a $36 billion-a-year industry. It lowers the cost and cuts the time for purification from days to hours.

Part of the cost savings come from eliminating the need for disposal since no toxic chemicals are used.

In November 2006, Allied Minds, a Boston-area company that invests in successful early stage technology, purchased the license, formed Purtein, LLC, and invested $500,000.

James Linder, M.D., president of UNeMed, said the venture with Allied Minds is an exciting one. "We see the partnership as a fast, effective way to commercialize this novel technology."

DR. BEDOWS DRAWS BLOOD FROM A FEMALE TIGER AT THE ZOO WITH THE HELP OF KEEPER HANNAH SAVORELLI.

"That's the beauty of the invention," said Chris Silva, CEO of Allied Minds and Purtein. "They created a way of purifying proteins in a novel and economical manner that brings down the cost."

Even before licensing the technology, Dr. Bedows was using it to help the Henry Doorly Zoo in Omaha. He, Doug Armstrong, D.V.M., associate director for medicine research, and Naida Loskutoff, Ph.D., reproductive physiologist, at the Henry Doorly Zoo, have been collaborating since 1994 on the zoo's assisted reproduction program to manage the genetic diversity in zoo animals.

In 2005, Dr. Bedows used the technology to engineer and purify new tiger hormones to stimulate ovulation for *in vitro* fertilization in order to reproduce endangered tigers. The purified hormones appear to be far superior to hormones currently used from humans, cattle or pigs. Hormones from humans, cattle and pigs can produce an unwanted immune system response in tigers.

"When you introduce a foreign matter, it might work the first time, but after that, the immune system may destroy it. Sterilization is one concern," Dr. Armstrong said.

"We are building new tiger hormones and purifying them in high enough quantities so the zoo can start using tiger hormones for *in vitro* fertilization and assisted reproduction," Dr. Bedows said. "What they get is a tiger hormone that is so genetically similar that the tiger recognizes the hormone as its own, thereby avoiding potential side effects."

The team is testing small amounts of tiger hormones on cell cultures in the laboratory and preliminary results show the technology works.

"The next step is to produce enough hormones to try it in a tiger," Dr. Armstrong said. "If it works, we'll gear up a whole system to produce enough hormones for our zoo, and also share them with others. There are only a couple of places in Europe that have attempted assisted reproduction with tigers. We've heard of no one else who has invested effort and resources to produce big cat hormones."

After 30 years in the laboratory, Dr. Bedows was reminded that surprises in basic research are impossible to ignore.

"It turns out, much to my chagrin, that the technology to advance our research was more valuable than the research itself – we got more funding for the technique than for the scientific data we produced," Dr. Bedows said.

Dr. Bedows explains his research in a video at www.unmc.edu/discover