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## Hauptman closer to breast cancer cure

Business First of Buffalo - by [Tracey Drury](#) Business First

A Buffalo researcher at **Hauptman-Woodward Medical Research Institute** has moved a step closer to a cure, and possibly the prevention, of the most common type of breast cancer.

Debashis Ghosh, a senior research scientist, reached a milestone by determining the third and last structure of an enzyme used by the human body to create estrogen, work that will enable further research to develop drugs to specifically target estrogen-dependent tumors in breast cancer.

Identifying the third enzyme culminates 40 years of research at Hauptman-Woodward, first begun by Yoshio Osawa and continued by Ghosh for the past 15 years. To Ghosh, the findings are just the beginning.

"This is what I've been waiting for," he says. "People have been trying to crystallize this enzyme for the last 35 years."

"There's a whole universe ahead of us," he says. "When people tell me that we have achieved our goal, I have a completely different view: I think our science is just beginning and what we can do is almost limitless. It's like being in Buffalo and winning the Super Bowl."

Ghosh's research on the aromatase enzyme will be featured this week in the scientific journal *Nature*. He also was keynote speaker last month at the ninth International Aromatase Meeting in Shanghai, China, which drew scientists from around the world.

The work was further confirmed last week by a four-year, \$2 million **National Institutes of Health** grant through the **National Institute of General Medical Sciences**.

Breast cancer remains the second-leading cause of cancer death in women. Though there are different types, more than 75 percent of all breast cancer tumors are estrogen-fed. Both men and women have some percentage of estrogen in their body.

The completion of the third enzyme structure follows Ghosh's work on the first structure in 1996 and the second in 2003. Ghosh's findings are significant, as knowing all three structures of the enzyme opens the door to customized, comprehensive medical treatment, says Walter Pangborn, executive vice president at HWI.

"This means that results from this research will form the basis for novel breast cancer drugs that are highly specific for aromatase, but cause minimal side effects," he says.

Though several drugs are approved by the **Food & Drug Administration** to treat breast cancer, the drugs prevent estrogen receptors from functioning. They also do not discriminate on what they target in the body, which results in a range of side effects.

A better outcome, Ghosh says, would be to reduce the amount of estrogen levels in the first place, which is accomplished with estrogen inhibitors. It is this excess estrogen that acts like a toxin and feeds breast tumors. Several large clinical trials have established unequivocally that aromatase inhibitors are more superior to antagonist drugs such as Tamoxifen, he says.

"This is why I think we are more excited. We will be trying to replace or make better drugs than are being used today," Ghosh says. "This has been a dream for many pharmaceutical companies to get the structure of the active side, then look inside and see how to design the key to open that lock. That is the idea behind structure-based rational design of drugs. You design a drug and make a drug that only binds to that one specific molecule and leaves everything else untouched."

Ghosh will continue his work now to design drugs to treat breast cancer, as well as vitamins or other drugs that could prevent the disease. In addition to his team at Hauptman-Woodward, he will work with researchers at **Roswell Park Cancer Institute**, where he holds a joint faculty appointment as associate member of the department of

pharmacology and therapeutics. He'll also work with Huw Davies, an organic synthetic chemist who moved from the University at Buffalo to **Emory University** six months ago.

Ghosh, who also studies macular degeneration and immunology, plans to spend the next five years patenting the aromatase work, developing the drugs and taking them to phase one clinical trials. He's fairly certain the pharmaceutical companies will be interested in licensing the drugs at that point.

"We cannot compete with the kind of resources the pharmaceutical companies have. We better use their resources in development for the benefit of everyone," he says. "The bonus here is that I have the opportunity now to go take it to really where it matters: to bring it to the benefit of mankind."

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