In the 1940s, women had one chance in 14 of getting breast cancer. Now it’s one in 8, says David Sherr.
Corralling Cancer

Zeroing in on a chemical that could halt breast cancer’s spread

By Rich Barlow

The photo collection snaking across two walls in David Sherr’s office includes a picture of a woman, her back to the camera, cradling a small child as they both scan the horizon. That snapshot of a second captures the pain of a lifetime, showing Sherr’s late wife, before she was diagnosed with the multiple myeloma that killed her a dozen years ago, holding their daughter.

“I have trouble putting that one of her up,” admits Sherr. “I’ve got to focus in here.” That’s because the School of Public Health professor of environmental health believes he’s zeroing in on a chemical that might halt metastasizing breast cancer cells and make it easier for surgeons to remove them. His wife’s death adds fuel to his quest for a therapy for breast cancer, which annually kills an estimated 40,000 women and about a 10th as many men, trailing only lung cancer as the most lethal form of the disease among women.

Sherr’s work is promising enough to have won one of BU’s $50,000 Ignition Awards two years ago, money that paid for experiments demonstrating two possible chemical inhibitors of cancer cells. Now, he and his lab are seeking research money from a Dutch biotech company for the lengthy and expensive process of testing these potential drugs on lab animals, the run-up to human trials.

Bottom line: even if everything pans out, any available therapy is likely a decade away. Still, what Sherr, who is also a School of Medicine professor of pathology and laboratory medicine, has seen under the microscope heartens him, and it begins with a protein, the aryl hydrocarbon receptor (AhR).

Thanks in part to research funded by the Art beCAUSE Breast Cancer Foundation, cofounded and directed by Ellie Anbinder (SED’62), scientists believe AhR is a prime culprit in the metastasizing of breast cancer. It signals cancer cells to lose their “Velcro,” Sherr’s metaphor describing the gene that pulls the cells together in one location, and it orders them to make enzymes that gobble up the environment around them.

Sherr believes that if we could neutralize AhR’s effects, we could halt the metastasis, making breast cancer a disease that can be lived with.

In the 1940s, a woman had a one in 14 chance of developing breast cancer over her lifetime; today, says Sherr, it’s one in 8. One theory for the higher risk is that modern life exposes us to more carcinogens, a notion supported by research associating exposure to chemicals like dioxins with breast cancer. (Less than 10 percent of breast cancers come from genetic susceptibility to the disease, he says.) Those chemicals activate Sherr to do its dirty work, which drew Sherr’s attention. Knowing what chemicals turned on AhR allowed Sherr and his colleagues to guess at the molecular structure of possible modulators for the protein. A computer search of more than one million molecules narrowed the possibilities, but they had to slog through more than 3,000 compounds before finding 3 chemicals they thought might do the trick.

They observed cancer cells in a tissue culture, doing what cancer does in a human body: invading and stretching out in tendrils to form oddball geometric shapes. Once the modulators are introduced, however, the cancer cells cluster together in tidier, rounder colonies, “like putting a fence around” them, says Sherr.

“Because they’re all sticking together, cancer cells cannot find their way across the tissue into a blood vessel and metastasize to some distant place,” he says, like the brain, liver, or bones. “It’s that metastatic cancer that kills you.” Also, “If you’re a surgeon...as long as the tumor is contained, no problem—’I cut it out, I zap it with radiation.’”

Sherr hopes that any drug he devises might combat other cancers, notably that of the brain, a hellishly difficult disease to treat. One study suggests the same receptor is at play there as well, says Sherr, who suspects the receptor helps fuel other aggressive cancers, too.