Implanting tumor control

By Michael J. Haas, Senior Writer

Researchers from Massachusetts and Texas have shown that implants of gelatin matrices embedded with endothelial cells decreased tumor growth and invasiveness in mice.¹ **Pervasis Therapeutics Inc.**, which developed the technology, has licensed the findings and is developing the implants to treat solid tumors in conjunction with surgical resection. A key question will be how long the implanted cells retain their function at the tumor site.

Over the past two decades, studies have shown that endothelial cells maintain vascular homeostasis by suppressing cellular proliferation, inflammation and angiogenesis. Conversely, dysfunctional endothelial cells can stimulate these processes and contribute to vascular disease or injury.

Based on those findings, the Massachusetts-Texas team hypothesized that normal and dysfunctional endothelial cells played similarly complex and opposing roles in the tumor microenvironment.

To test that hypothesis, the researchers cultured human breast and lung cancer cell lines in media conditioned with normal human endothelial cells. The cancer cells had less growth and invasiveness *in vitro* and induced less tumorigenesis and metastasis in mice than cell lines cultured in control media.

Next, the team cultured human aortic endothelial cells in gelatin sponge matrices—the same technology Pervasis is developing under the name Vascugel—and implanted the matrices near the tumors of mice with lung cancer xenografts. The implants decreased tumor growth and invasiveness compared with acellular control implants.

“Even to the untrained eye, tumors treated with the implants are visibly more structurally intact and less ragged in appearance than untreated tumors,” which could make treated tumors more amenable to surgical resection or more sensitive to radio- or chemotherapy, team lead Elazer Edelman told *SciBX*.

The implants also could be used after surgical resection to kill any residual cancer cells, thereby preventing tumor recurrence or metastasis “so that surgeons don’t have to excise such a wide tissue margin” during resection, he said.

Additionally, said Edelman, the matrix-embedded cells are safer

and more readily controlled than freely injected cells would be.

“Endothelial and most other solid cells require some type of physical support, such as a basement membrane, for normal function. Cells injected without some kind of support will function abnormally and always cause immune responses in the host because the cells are not in their normal *in vivo* environment,” he said.

According to Edelman, the matrix component of the implant mimics that normal environment—thereby enabling normal cellular functions and preventing host immunological responses—and it allows the cells to be introduced exactly where they are needed.

Edelman is a professor of health sciences and technology at the **Massachusetts Institute of Technology (MIT)**, professor of medicine at **Harvard Medical School** and a coronary care unit cardiologist at **Brigham and Women’s Hospital**.

He is also a cofounder of Pervasis and member of the company’s board of directors and scientific advisory board.

Edelman’s team included scientists from the **Boston University School of Medicine** and **The University of Texas at Austin**. Data were reported in *Science Translational Medicine*.¹

The study adds “another piece to the tumor microenvironment puzzle by showing that the introduction of normal cells into the tumor environment—or getting the dysfunctional cells already present there to adapt some semblance of normal function—could be one way to treat tumors,” said Adrian Shieh, assistant professor of biomedical engineering at **Drexel University**.

Shieh agreed that the near-term application of the findings is implanting endothelial cell matrices after excision of the primary tumor. He noted that the approach takes advantage of the cross talk between normal and cancerous cells in one direction, “but the cross talk occurs in the other direction, too, and could cause the normal cells to be transformed by the tumor cells.”

Thus, Shieh told *SciBX*, “by far the biggest question—and the make-or-break issue for any approach that introduces normal cells to treat tumors—is how long the normal cells will remain normal in the presence of the tumor or residual tumor cells.”

The transformation of normal cells “will probably happen in time. The question is whether you can prevent it” so that the implanted cells remain functionally normal for as long as necessary to treat the cancer, he said.

Edelman said the team’s ongoing work includes determining how long the implanted cells retain normal functions at the tumor site and whether those functions can be prolonged during cancer treatment.

Normal behavior

Pervasis has licensed the new findings from MIT and is developing PVS-30200, which consists of allogeneic human aortic endothelial cells cul-

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tured in **Pfizer Inc.**'s Gelfoam sponge matrix and implanted after surgical resection to prevent the recurrence and metastasis of solid tumors. The product is in preclinical development.

The company "is actively talking to major oncology companies that have an expertise in drug development and an interest in local therapy approaches to treat cancer" to develop PVS-30200, Edelman said.

Internally, Pervasis is focused on using Edelman's technology in the vascular disease space. The company was founded in 2003 on technology in-licensed from MIT that is now in clinical development under the name Vascugel.

Vascugel has completed two Phase II trials in patients with end-stage renal disease (ESRD) undergoing placement of an arteriovenous graft or fistula for hemodialysis access.

The company plans to begin a Phase III trial this year, according to Pervasis president and CEO Frederic Chereau.

Pervasis also is developing PVS-10200, an injectable formulation of allogeneic aortic endothelial cells cultured in Gelfoam powder. It

is in a Phase I/II trial to treat restenosis in patients with peripheral artery disease (PAD).

Pfizer markets Gelfoam gelatin absorbable sponge and powder as a hemostatic agent.

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