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Making Cancer Feel the 'Heat' Via Immune-Targeted Vaccine

By Jennifer Boggs Assistant Managing Editor

A half-dozen biotechs are in the clinic with heat- shock protein (Hsp)-based drugs, but 2008 start-up Heat Biologics is putting a twist on that approach by developing Hsp vaccines capable of inducing and maintaining immune responses against cancer and other diseases.

Hsps have “never been utilized this way,” said Jeff Wolf, the company’s founder and chairman.

The technology, named ImPACT (Immune Pan Antigen Cytotoxic Therapy), stems from the laboratory of Eckhard Podack, professor of microbiology and immunology at the University of Miami, Miller School of Medicine, and is based on Hsp gp96, a chaperone protein that mobilizes and activates killer T cells to fight cancer.

Hsp gp96 is a folding protein that “comes into contact with every protein that cell produces,” Wolf said.

Normally, it’s “leashed” to cells by the KDEL sequence, which prevents it from leaving the endoplasmic reticulum. And, when cells undergo necrosis, or unnatural cell death, they release Hsp gp96, as well as any Hsps that were being folded at the time, and create an immune response.

“The idea is to take a cell, sever this leash that ties gp96 to the cell and enable gp96 to freely secrete from the cell,” Wolf told BioWorld Today. “So cells continuously pump out gp96 to generate an immune response.”

Heat is targeting non-small-cell lung cancer as its first indication. In that case, the company has taken a lung cancer cell line that was removed from a patient about 10 years ago – the cancer, naturally, irradiated so that it can’t replicate – and modified it so that it secretes gp96.

The off-the-shelf product, designated HS-L1, then is injected into the NSCLC patient, where the cells live for several days, constantly secreting the gp96 protein to help the immune system generate a pan antigen immune response. Basically, “it stimulates what the cancer cells would produce if they were not immune-suppressed,” Wolf said.

Heat’s work so far has shown twice-weekly injections for 18 weeks as the most promising dosing regimen. The company is testing HS-L1 in a Phase I/II trial in NSCLC patients, with a primary endpoint of safety and secondary endpoints testing progression-free survival, overall survival and immune response to the drug.

To date, HS-L1 has only been tested as a monotherapy, but Wolf said there’s a chance it could work well with targeted therapies. But because it requires a strong immune system, combining with

chemotherapy is out of the question. “We want patients with active immune systems, so they have to be chemotherapy-free for 30 days” prior to treatment with HS-L1, he said.

Beyond NSCLC, other cancers will follow. Heat anticipates moving into the clinic with a bladder cancer program in the first quarter of 2012 and an ovarian cancer program in the second quarter of next year. “There’s a whole pipeline we can develop using this approach,” Wolf added.

And the ImPACT technology’s use isn’t limited to cancer. It also has applications in viral diseases. “In some ways, we look at the platform as an antigen delivery technology,” he said. But, unlike the programs in cancer, researchers working on viral diseases don’t start out with the disease cell lines; instead, they would create a cell line and then infuse it with specific antigens. For instance, initial work in viral diseases has focused on SIV, the primate version of HIV. “In this case, we start with fibroblast cell lines and transfect antigens for SIV,” Wolf said.

A feasibility study demonstrated promising cytotoxic T-cell responses in primates, and the approach now is being studied in another nonhuman primates trial funded by the National Institutes of Health (NIH). That trial is part of a collaboration between the University of Miami and the Experimental Immunology Branch at NIH.

Heat has a second platform, an antibody technology that could one day be used in combination with ImPaCT. That platform includes an antibody against TNFR25, a protein that stimulates regulatory T-cell expansion and proliferation.

Candidates emerging from that platform could be aimed at indications such as transplantation, asthma or “any time you need to regulate – up or down – the Tregs of the immune system,” Wolf said.

He said it would be a couple of years before Heat moves into the clinic with that technology. And it’s likely the firm will look to partner, since there are large disease markets involved.

For its initial program in cancer, Heat has more options, even the possibility of taking the lead program to market on its own. Heat has not disclosed its funding to date, but Wolf said, “we’re in pretty good shape” financially, though the company expects its expenses to increase as it reaches Phase II trials and beyond.

Heat has about 10 employees and is looking to expand. The company, based in Miami, also plans to open a corporate office in Research Triangle Park, N.C. ■

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