NEOANTIGENICS: OOZYTE OVERSIGHT

By Emily Cukier-Mesnier, Senior Writer

Neoantigenics LLC is developing cancer diagnostics and therapeutics based on oocyte-specific proteins that are re-expressed in some cancers. The goal is to create therapies with lower potential to cause side effects, including infertility.

For premenopausal women, many types of cancer treatment, such as chemotherapy, radiotherapy and hormonal treatments, can cause premature menopause or temporary or permanent infertility.

Neoantigenics hopes to overcome that problem by developing therapies whose biologic target is normally confined to maturing oocytes, so that fertility is only impaired for the duration of treatment.

CEO Brian Pollok said Neoantigenics was formed to develop work from the lab of co-founder John Herr, who studies gamete-specific protein expression on egg and sperm cells. Herr is a professor of cell biology and biomedical engineering at the University of Virginia.

Herr has identified several proteins that are normally only expressed on oocytes during specific developmental stages, but become re-expressed in some transformed tissues.

Pollok said these proteins were not included in standard microarrays used to profile gene expression in human cancers, that they were not identified as cancer biomarkers until specifically looked for.

Pollok said he is not aware of another company targeting oocyte antigens to treat cancer.

The company's primary target is the astacin-like metallo-endoproteinase M12 family protein (SASIB; ASTL, ovastacin), an enzyme released from eggs after fertilization to help prevent polyspermy.

SASIB is also widely expressed in epithelial cancer.

Pollok said it's not known why it is advantageous for cancer cells to re-express SASIB, but that the protein is expressed on the cell surface and becomes internalized upon mAb binding. Thus, it can serve as a marker for cancer diagnostics or a target for delivery of cytotoxic payloads by antibody-drug conjugates (ADCs).

Pollok said SASIB expression on cancers varies both between and within patients; however, it occurs on almost 100% of serous ovarian cancers. It may also correlate with cancer aggressiveness.

"The less differentiated the cancer cell appears to be, the more likely it is to express the antigen," he said.

He added that because normal SASIB expression is restricted to late stages of oocyte development, "the antibody-drug conjugate may interact with a mature egg, or a released egg, but it should not affect the egg reserve. So once the ADC is cleared, the woman should still maintain fertility."

Despite the antigen's association with oocytes, Pollok said non-gender-specific cancers in men and women may express the antigen.

Pollok said the virtual company is using CROs to generate its mAbs, and will use Herr's lab to select the preferred mAb and indication via a battery of xenograft models of cancers that express SASIB, including ovarian, renal, uterine and pancreatic cancers.

He said the company plans to raise a series A round in mid-2015 to fund contract work to create an ADC to generate POC data to attract a partner.

One potential source for ADC technology is Pfizer Inc., which owns a single-digit percentage stake in Neoantigenics and is collaborating on R&D. The pharma does not have rights to the company's IP or rights of first negotiation to its discoveries.

Pollok said the final choice of conjugate and ADC platform would rest with the partner, which would be responsible for securing the IP for the ADC.

Neoantigenics' IP is licensed exclusively from the University of Virginia and covers diagnostic and therapeutic uses of SASIB. The company has an option to license additional cancer-associated oocyte targets identified by Herr's research.

Pollok said Neoantigenics' mAbs also could be used in chimeric antigen receptor (CAR) T cell therapies, which could be developed with a different partner than the ADCs. He said the company's programs were in early discovery for this use.

In addition to its investors, Neoantigenics has raised over $1.2 million in grants from organizations including the Center for Innovative Technology, University of Virginia Licensing & Ventures Group and the Wallace H. Coulter Foundation.

Neoantigenics is also working on immunohistochemical and quantitative PCR assays to detect SASIB. Pollok said the company has not yet decided whether it will develop a companion diagnostic independently or with a partner.

Companies and Institutions Mentioned:
Center for Innovative Technology (CIT), Herndon, Va.
Neoantigenics LLC, Charlottesville, Va.
Pfizer Inc. (NYSE: PFE), New York, N.Y.
University of Virginia, Charlottesville, Va.
Wallace H. Coulter Foundation, Miami, Fla.