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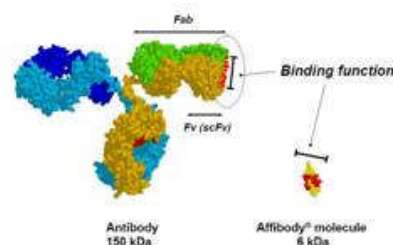
## Imaging Technique Allows Researchers to Monitor Protein Changes in Mouse Tumors

A new imaging technique can monitor, in living mice, the HER2 protein found in above-normal amounts in many cases of breast cancer as well as some ovarian, prostate and lung cancers. This new approach, once validated in mice and pending further experiments, could provide a real-time noninvasive method for identifying tumors in humans who express HER2 and who would be candidates for targeted therapy directed against this protein. It may also provide real-time information that will help clinicians optimize treatment for individual patients. The study, published in the July 2009 issue of *The Journal of Nuclear Medicine*, was conducted by researchers at the National Cancer Institute (NCI) and the National Institute of Biomedical Imaging and Bioengineering, both parts of the National Institutes of Health.

The HER2 protein is overexpressed (produced at higher-than-normal levels) in approximately 20 percent to 25 percent of breast cancers. Tumors that overexpress HER2 are more aggressive and more likely to recur than tumors that do not overexpress the protein. Targeted therapies directed against HER2 can slow or stop the growth of tumors that overexpress it.

Currently, HER2 expression is measured in biopsy specimens - that is, in tumor samples that have been removed from the body. However, expression of HER2 in these samples may not accurately represent HER2 expression in the tumor as a whole. Moreover, follow-up biopsies are not routinely performed after the initial diagnosis, and there are no means to evaluate how long a targeted therapy takes to reach its target, how effective it is, and how long its effects last.

In this study, the research team used an imaging compound that consists of a radioactive atom (fluorine-18) attached to an Affibody molecule, a small protein that binds strongly and specifically to HER2. Affibody molecules, developed by Affibody AB, Bromma, Sweden, are much smaller than antibodies and can reach the surface of tumors more easily. The radioactive atom allows the distribution of the Affibody molecules in the body to be analyzed by positron emission tomography (PET) imaging.



Affibody<sup>®</sup> molecules are much smaller than antibodies or antibody fragments, but the size of their binding surfaces are comparable.

The research team first used the radiolabeled Affibody molecule to visualize tumors that expressed HER2 in mice. The mice were injected under the skin with human breast cancer cells that varied in their levels of HER2 expression, from no expression to very high expression. After three to five weeks, when tumors had formed, the mice were injected with the Affibody molecule and PET images were recorded. The levels of HER2 expression as determined by PET were consistent with the levels measured in surgically removed samples of the same tumors using established laboratory techniques.

To determine whether their method could be used to monitor possible changes in HER2 expression in response to treatment, the team next injected the Affibody molecule into mice with tumors that expressed very high or high levels of HER2 and then treated them with the drug 17-DMAG, which is known to decrease HER2 expression. PET scans were performed before and after 17-DMAG treatment. The researchers found that HER2 levels were reduced by 71 percent in mice with tumors that expressed very high levels of HER2 and by 33 percent in mice with tumors that expressed high levels of HER2 in comparison with mice that did not receive 17-DMAG. The researchers confirmed these reductions by using established laboratory techniques to determine the concentrations of HER2 in the tumors after they were removed from the mice.

"Our work shows that PET imaging using Affibody molecules was sufficiently sensitive to detect a twofold

to threefold decrease in HER2 expression," said senior author Jacek Capala, Ph.D., of NCI's Center for Cancer Research. "Therefore, PET imaging may provide a considerable advantage over current methods. Our technique would allow a better selection of patients for HER2-targeted therapies and also early detection of tumors that either do not respond to or acquire resistance to these therapies."

"This approach might easily be extended to forms of cancer other than breast cancer," continued Capala. "Because Affibody molecules may be selected to target specific cell proteins, similar compounds can be developed to target proteins that are unique to other types of tumors."

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For more information on Dr. Capala's research, please go to <http://ccr.cancer.gov/staff/staff.asp?profileid=9891>.

NIBIB, a component of NIH, is dedicated to improving health by bridging the physical and biological sciences to develop and apply new biomedical technologies. Additional information and publications are available at <http://www.nibib.nih.gov>.

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**Reference:** Kramer-Marek G, Kiesewetter DO, and Capala J. HER2 expression changes in breast cancer xenografts following therapeutic intervention can be quantified using PET imaging and <sup>18</sup>F-labelled Affibody molecules. *J. Nucl. Med.* Vol. 50, No. 7.