Sources: Dolores Takemoto, 785-532-7009, dtak@k-state.edu; and Thu Annelise Nguyen, 785-532-4429, tanguyen@k-state.edu http://www.k-state.edu/bchem/fac/dt/main2.html http://www.vet.k-state.edu/depts/dmp/personnel/faculty/anguyen.htm
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K-STATE BIOCHEMISTRY PROFESSOR DISCOVERS LINK BETWEEN LOW OXYGEN LEVELS IN BODY AND CANCER-AIDING PROTEIN; COULD HELP TREATMENTS FOR RETINOBLASTOMA AND BREAST CANCER

MANHATTAN -- What began as research into how diabetics could possibly preserve their eyesight has led to findings that could prolong the vision of children afflicted with retinoblastoma.

Dolores Takemoto, a Kansas State University professor of biochemistry who was researching protein kinase C gamma in the lens of the human eye, found her work taking a fascinating turn when she discovered a correlation between the protein Coonexin46 and hypoxia -- a deficiency of oxygen which kills normal tissue cells.

According to the data, Coonexin46, or Cx46, appears in the body during these levels of low oxygen. Besides the eye, which is one of the body's only naturally occurring hypoxic tissue, Cx46 also is present in cancer cells since the cells seal themselves off from the oxygen carried by the blood vessels, thus creating a hypoxic environment.

Takemoto believes the findings will lead to serious advancements in treating retinoblastoma, a cancer that forms in the tissue of the retina -- the light-sensitive layers of nerve tissue on the back of the eye. It occurs in 300 U.S. children under the age of 5 each year, according to the National Cancer Institute.

"When a child comes in with retinoblastoma in one eye it's usually too late in the process to save that eye, and, it will spread to the other eye," Takemoto said.

Once an eye becomes cancerous, it has to be removed to prevent the tumor from spreading. Too often, though, Takemoto said, by the time the tumor is noticed in one eye, it has already spread to the second, resulting in a child being permanently blind.

Through her research, Takemoto believes a siRNA medication can be invented which can be injected monthly into the noncancerous eye, preventing tumor growth. siRNA, or small interfering ribonucleic acid, is a class of double-stranded RNA molecules that can be used to interfere with the expression of a specific gene. In this case, the siRNA would suppress Cx46, which allows a tumor to exist in a hypoxic environment. In this manner, the tumor can be prevented from growing at the early hypoxic stage.

Using a mouse model for retinoblastoma, the Takemoto lab has found that use of siRNA to lower the levels of Cx46 will prevent tumor formation.

An international application has been filed with the Patent Cooperation Treaty regarding the findings.

During her trials with Cx46, Takemoto collaborated with Thu Annelise Nguyen, associate professor of toxicology at K-State. The two examined biopsies of MCF-7 breast cancer, where they also found Cx46 present. Takemoto said the same was true for samples of colon cancer.

"Any time there's a drop in oxygen within the body, Cx46 appears," Takemoto said.

While Takemoto's research into Cx46 is focused on the eye, Nguyen is studying Cx46 in breast cancer. She is currently exploring drug discovery and drug testing related to breast cancer.

Besides treating tumors, Takemoto said she believes these findings could help with treatment in acute or chronic heart disease, heart attacks, retinal ischemia, ischemia of the brain, blood pressure problems and glaucoma, as well as for health applications in animals.

Findings have been published in an online edition of the International Journal of Cancer, "A novel role of gap junction connexin46 protein to protect breast tumors from hypoxia." Publication in a printed edition will follow.

Takemoto has recently been named a Fellow of the Association for Research in Vision and Ophthalmology. She will present her data in May at an association conference, where hers will be one of the highlighted talks.

Takemoto's research was made possible by a grant of more than $366,000 from the National Eye Institute in fall 2009.