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ADAM-12 gene could hold key to cancer, arthritis and cardiac treatments

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ADAM-12 is not only the name of a 1970's television police drama – it's also the gene that University of Missouri researchers believe could be an important element in the fight against cancer, arthritis, and cardiac hypertrophy, or thickening of the heart's walls.

Alpana Ray, research associate professor in the MU College of Veterinary Medicine, and a team of researchers including Bimal Ray, professor of Veterinary Pathobiology, have been studying the ADAM family of genes for several years. Alpana Ray's latest publication in the *Proceedings of the National Academy of Sciences* (*PNAS*) discusses one pathway by which the ADAM-12 gene could be regulated, a process that could eventually be used as part of a treatment plan.

Scientists know that ADAM-12 is normally found in very low levels in adults, but during cancer, arthritis and cardiac hypertrophy, ADAM-12 level goes up. The only time it is normal to find a high level of the gene is during pregnancy, when ADAM-12 can be found in the placenta.

At the molecular level, Ray's team found a Z-DNA-binding silencer element that keeps the level of ADAM-12 low in normal conditions. They believe that if they could alter Z-DNA-binding silencer, new therapies could be right around the corner.

"We are finding that in the placenta, where ADAM-12 is highly expressed, the repressor protein (Z-DNA-binding protein) is inactive. In other tissues, where ADAM-12 expression is low, the repressor is

active," Alpana Ray said. "What we don't know is how it actually works. We know co-factors are at work here. If we can identify the class of proteins that interact with Z-DNA repressor, it could lead to many therapeutic applications."

Because ADAM-12 is a versatile gene, it may play a role in metastasis during which cancer cells travel throughout the body and spread to other organs.

"We know that ADAM-12 causes cells to anchor to one another, and we know that ADAM-12 allows cancer cells to proliferate," said Alpana Ray.

Bimal Ray notes that the next phase of the work would be to determine how the Z-DNA-binding protein works.

"Most of the success in cancer therapy lies in a combination of approaches and chemotherapies, and this could become another piece of the puzzle that leads to the cure," Bimal Ray said.

Provided by University of Missouri-Columbia