MedicalXpress

MicroRNA that blocks bone destruction could offer new therapeutic target for osteoporosis

June 25 2014

UT Southwestern cancer researchers have identified a promising molecule that blocks bone destruction and, therefore, could provide a potential therapeutic target for osteoporosis and bone metastases of cancer.

The molecule, miR-34a, belongs to a family of small molecules called microRNAs (miRNAs) that serve as brakes to help regulate how much of a protein is made, which in turn, determines how cells respond.

UT Southwestern researchers found that mice with higher than normal levels of miR-34a had increased bone mass and reduced bone breakdown. This outcome is achieved because miR-34a blocks the development of bone-destroying cells called osteoclasts, which make the bone less dense and prone to fracture.

"This new finding may lead to the development of miR-34a mimics as a new and better treatment for osteoporosis and cancers that metastasize to the bone," said senior author Dr. Yihong Wan, Assistant Professor of Pharmacology and member of the UT Southwestern Harold C. Simmons Cancer Center.

Her team found that injecting nanoparticles containing an artificial version, or mimic, of miR-34a into a mouse with post-menopausal osteoporosis decreased bone loss. "Interestingly, the mouse miR-34a is

identical to that in humans, which means that our findings may apply to humans as well," said Dr. Wan, Virginia Murchison Linthicum Scholar in Medical Research at UT Southwestern.

The study is published online in the journal *Nature*.

High levels of bone destruction and reduced bone density caused by excessive osteoclasts are characteristic of osteoporosis, a common bone disease in which bones become fragile and susceptible to fracture. This condition disproportionately affects seniors and women, and leads to more than 1.5 million fractures annually.

miR-34a could have an additional therapeutic application, offering protection from bone metastases in a variety of cancers, Dr. Wan noted. Bone metastases happen when cancer cells travel from the primary tumor site to the bone, establishing a new cancer location. Researchers saw that injecting the miR-34a mimic in mice could prevent the metastasis of breast and skin cancer cells specifically to bone, mainly by disarming the metastatic niche in bone.

Co-author Dr. Joshua Mendell, Professor of Molecular Biology at UT Southwestern and member of the UT Southwestern Harold C. Simmons Cancer Center, noted that his laboratory previously showed that miR-34a can directly suppress the growth of cancer cells.

"We were very excited to see, through this collaborative work with Dr. Wan's group, that miR-34a can also suppress bone metastasis. Thus, miR-34a-based therapy could provide multiple benefits for cancer patients," said Dr. Mendell, CPRIT Scholar in Cancer Research. CPRIT is the Cancer Prevention and Research Institute of Texas, which provides voter-approved state funds for groundbreaking cancer research and prevention programs and services in Texas.