Scientists engineer nanoparticles to prevent bone cancer, strengthen bones

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A research collaboration between Brigham and Women's Hospital (BWH) and Dana-Farber Cancer Institute (DFCI) has utilized nanomedicine technologies to develop a drug-delivery system that can precisely target and attack cancer cells in the bone, as well as increase bone strength and volume to prevent bone cancer progression.

The study is published the week of June 30, 2014 in *Proceedings of the National Academy of Sciences*.

"Bone is a favorable microenvironment for the growth of cancer cells that migrate from tumors in distant organs of the body, such as breast, prostate and blood, during disease progression," said Archana Swami, PhD, BWH Laboratory of Nanomedicine and Biomaterials, co-lead study author. "We engineered and tested a bone-targeted nanoparticle system to selectively target the bone microenvironment and release a therapeutic drug in a spatiotemporally controlled manner, leading to bone microenvironment remodeling and prevention of disease progression."

"There are limited treatment options for bone cancers," added Michaela Reagan, PhD, DFCI Center for Hematologic Oncology, co-lead study author. "Our engineered targeted therapies manipulate the tumor cells in the bone and the surrounding microenvironment to effectively prevent cancer from spreading in bone with minimal off-target effects."

The scientists developed stealth nanoparticles made of a combination of

clinically validated biodegradable polymers and alendronate, a clinically validated therapeutic agent, which belongs to the bisphosphonate class of drugs. Bisphosphonates bind to calcium. The largest store of calcium in the human body is in bones, so bisphosphonates accumulate in high concentration in bones.

By decorating the surface of the nanoparticles with alendronate, the nanoparticles could home to bone tissue to deliver drugs that are encapsulated within the nanoparticles and kill tumor cells, as well as stimulate healthy bone tissue growth. Furthermore, bisphosphonates are commonly utilized during the treatment course of cancers with bone metastasis, and thus alendronate plays a dual role in the context of these targeted nanoparticles.

The scientists tested their drug-toting nanoparticles in mice with multiple myeloma, a type of bone cancer. The mice were first pre-treated with nanoparticles loaded with the anti-cancer drug, bortezomib, before being injected with myeloma cells. The treatment resulted in slower myeloma growth and prolonged survival. Moreover, the researchers also observed that bortezomib, as a pre-treatment regimen, changed the make-up of bone, enhancing its strength and volume.

"These findings suggest that bone-targeted nanoparticle anti-cancer therapies offers a novel way to deliver a concentrated amount of drug in a controlled and target-specific manner to prevent tumor progression in multiple myeloma," said Omid Farokhzad, MD, director of the BWH Laboratory of Nanomedicine and Biomaterials, co-senior study author. "This approach may prove useful in treatment of incidence of bone metastasis, common in 60 to 80 percent of cancer patients and for treatment of early stages of multiple myeloma."

Added Irene Ghobrial, MD, DFCI Center for Hematologic Oncology, co-senior study author: "This study provides the proof-of-concept that

targeting the bone marrow niche can prevent or delay bone metastasis. This work will pave the way for the development of innovative clinical trials in patients with myeloma to prevent progression from early precursor stages or in patients with breast, prostate or lung cancer who are at high-risk to develop bone metastasis."

More information: Engineered nanomedicine for myeloma and bone microenvironment targeting, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1401337111

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