Osteoarthritis research in progeria mouse models reveals promising treatment combinations

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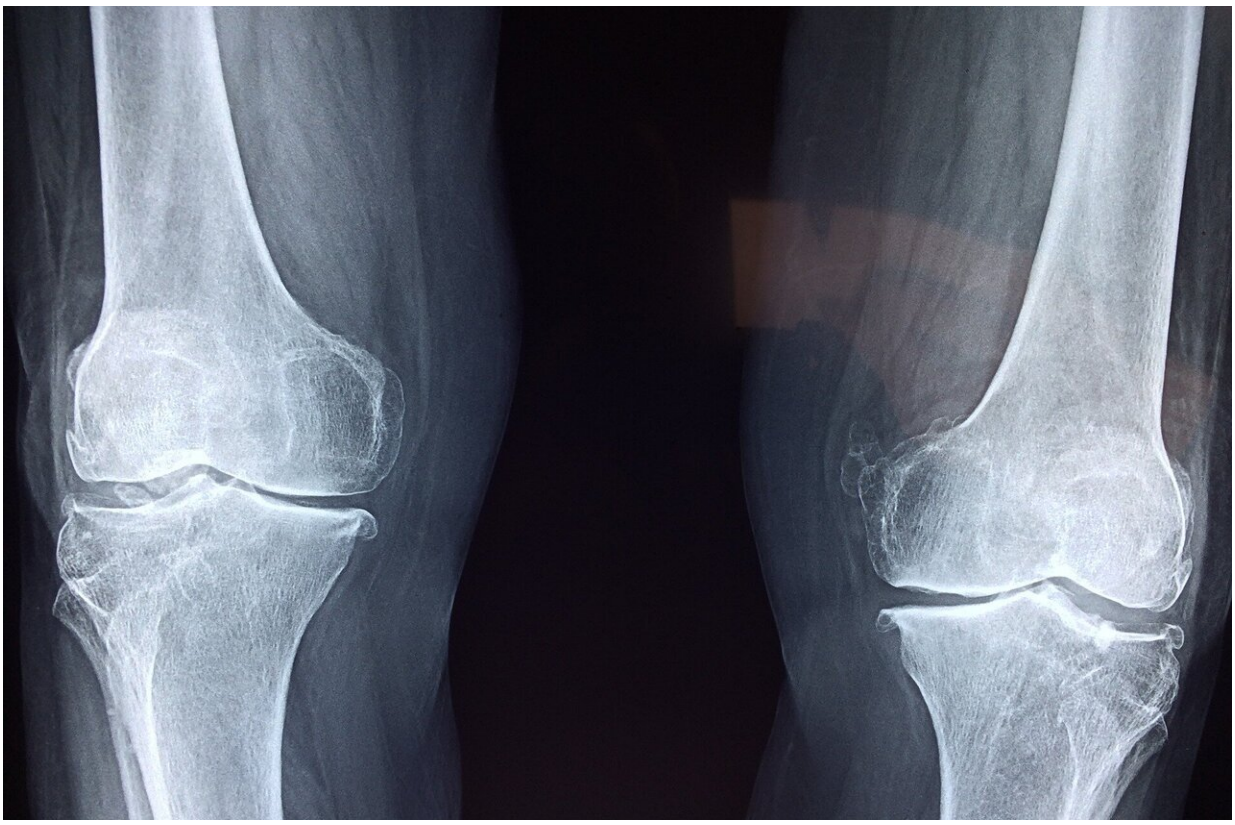

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Hutchinson-Gilford progeria syndrome (HGPS) is a fatal condition that is especially prevalent in the skin, cardiovascular and the

musculoskeletal systems. There exists a wide gap between existing knowledge of the disease and a potential treatment or cure.

In a study published today in the journal *Proceedings of the National Academy of Science*, researchers led by Ara Nazarian, Ph.D., a principal investigator in the Center for Advanced Orthopaedic Studies at BIDMC, investigated the musculoskeletal phenotype of the homozygous G608G BAC-transgenic progeria mouse model developed at Dr. Collins' lab at the National Institutes of Health, and determined the phenotypic changes of these mice after a five-arm preclinical trial of different treatment combinations with lonafarnib, pravastatin, and zoledronic acid.

"We observed that Lonafarnib did not improve bone or cartilage indices; however, treatment combinations with pravastatin and zoledronic acid significantly improved bone mechanical properties and cartilage structural parameters," said Nazarian.

The changes demonstrated in the cortical bone structure, rigidity and strength of the HGPS G608G mouse model may increase the risk for bending and deformation of bones, which could result in the skeletal dysplasia characteristic of HGPS. Cartilage abnormalities seen in this model resemble the changes observed in age-matched wild type animals, such as decreased cartilage thickness and volume. Such changes might mimic prevalent degenerative joint diseases in the elderly, including osteoarthritis (OA).

More animal studies will be necessary before investigating the ability of this disease model to help with OA studies. But Nazarian is optimistic about the possibilities offered by this animal model.

"Osteoarthritis is a chronic debilitating disease that degrades articular cartilage and is one of the most common causes of chronic disability and pain in the elderly," said Cubria, previously a postdoctoral fellow at

BIDMC and Harvard Medical School. "Accelerated aging animal models such as this mouse model could offer a meaningful opportunity to study degenerative joint diseases."

More information: Maria B. Cubria el al., "Musculoskeletal phenotype of the G608G progeria mouse model: A preclinical study with lonafarnib, pravastatin, and zoledronic acid," *PNAS* (2020). www.pnas.org/cgi/doi/10.1073/pnas.1906713117

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