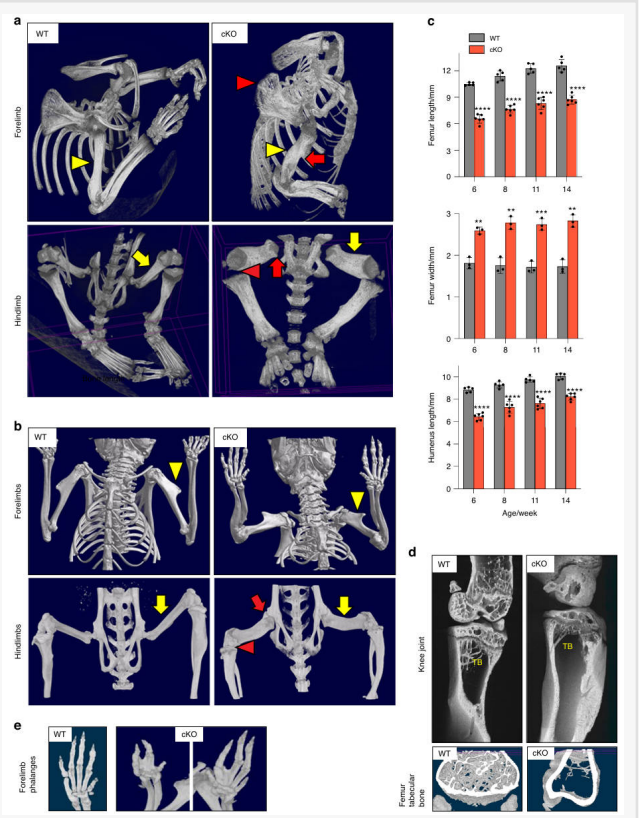
Skeletal health unraveled: the critical role of LRP1

TN, UNITED STATES, February 28, 2025 /EINPresswire.com/ -- A new study has unveiled the crucial role of low-density lipoprotein receptor-related protein 1 (LRP1) in skeletal development. Researchers have found that a deficiency of LRP1 in skeletal progenitor cells results in severe and lasting skeletal defects, including joint fusion, malformed bones, and impaired mobility. Further investigation revealed that LRP1 is a key regulator of the non-canonical Wnt/planar cell polarity (PCP) pathway, which is essential for proper bone formation. These findings not only deepen our understanding of bone biology but also open new avenues for targeted therapies to treat skeletal disorders.



Representative images of in vivo X-ray analysis of limbs of 2-week-old (a) and 14-week-old (b) WT and Lrp1flox/flox/Prrx1Cre homozygote conditional KO (cKO) mice.

Skeletal conditions such as developmental dysplasia of the hip (DDH), osteoporosis, and osteoarthritis affect millions worldwide, often causing chronic pain and disability. These disorders stem from complex genetic and environmental interactions that disrupt bone formation and joint development. Despite advances in treatment, effective interventions remain limited, highlighting the urgent need for research into the molecular mechanisms that govern skeletal development. Identifying critical proteins like LRP1 could be a key step toward novel therapeutic approaches.

A study (DOI: 10.1038/s41413-024-00393-x) published on January 26, 2025, in Bone Research, provides compelling new evidence of LRP1's essential role in bone development. Led by researchers at the University of Liverpool, the study demonstrates that LRP1 deficiency in skeletal progenitor cells leads to profound skeletal malformations. By uncovering how LRP1 influences bone formation at the molecular level, this research offers fresh insights into the origins of skeletal disorders and potential strategies for intervention.

Using a sophisticated conditional knockout mouse model, the research team explored the effects of LRP1 loss in skeletal progenitor cells. They discovered that LRP1 is highly expressed in these cells, particularly in the perichondrium—a critical layer for bone development. Mice lacking LRP1 exhibited severe skeletal abnormalities, including joint fusion, malformed cartilage templates, and delayed ossification, none of which were present in control mice. This striking contrast underscores LRP1's indispensable role in skeletal formation.

Further molecular analysis revealed that LRP1 interacts directly with Wnt5a, a key player in the non-canonical Wnt/planar cell polarity (PCP) pathway. By facilitating Wnt5a uptake and recycling, LRP1 ensures proper Wnt signaling—an essential process for bone formation and joint integrity. This discovery not only highlights LRP1's regulatory role in skeletal development but also establishes a direct link between Wnt signaling dysregulation and skeletal disorders.

"This study marks a significant leap in our understanding of bone formation," said Dr. Kazuhiro Yamamoto, a leading researcher on the project. "Our findings highlight the crucial role of LRP1 in regulating Wnt signaling, a key pathway essential for the development and maintenance of skeletal tissues. By identifying this mechanism, we have opened new possibilities for therapeutic interventions targeting skeletal disorders."

The potential applications of this research are vast. By elucidating LRP1's function, scientists may develop targeted treatments for conditions like DDH, osteoporosis and osteoarthritis, potentially improving outcomes for millions of patients. Moreover, a deeper understanding of skeletal development could lead to preventative strategies, reducing the incidence of bone-related disorders. As researchers continue to explore the intricate biology of skeletal health, discoveries like this pave the way for a future where bone diseases can be effectively managed or even prevented.

DOI
10.1038/s41413-024-00393-x

Original Source URL
https://doi.org/10.1038/s41413-024-00393-x

Funding information
This work was supported by the ministry of education of the Kingdom of Saudi Arabia (to M. Alhashmi), Libyan Ministry of Higher Education and Scientific Research and ECMage (to A.M.E. Gremida), Qatar National Research Fund (to N.A. Al-Maslamani), European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement (860635 to M. Antonaci and A. Kerr), BBSRC Grants (BB/T00715X/1 to S.K. Maharana and G.N. Wheeler; BB/X000907/1 to D.A. Turner), Versus Arthritis Career Development Fellowship (21447 to K. Yamamoto) and Versus Arthritis Bridging Fellowship (23137 to K. Yamamoto).

Lucy Wang
BioDesign Research
email us here