Changes to cartilage linked to bone cancer offers a possible new diagnostic approach

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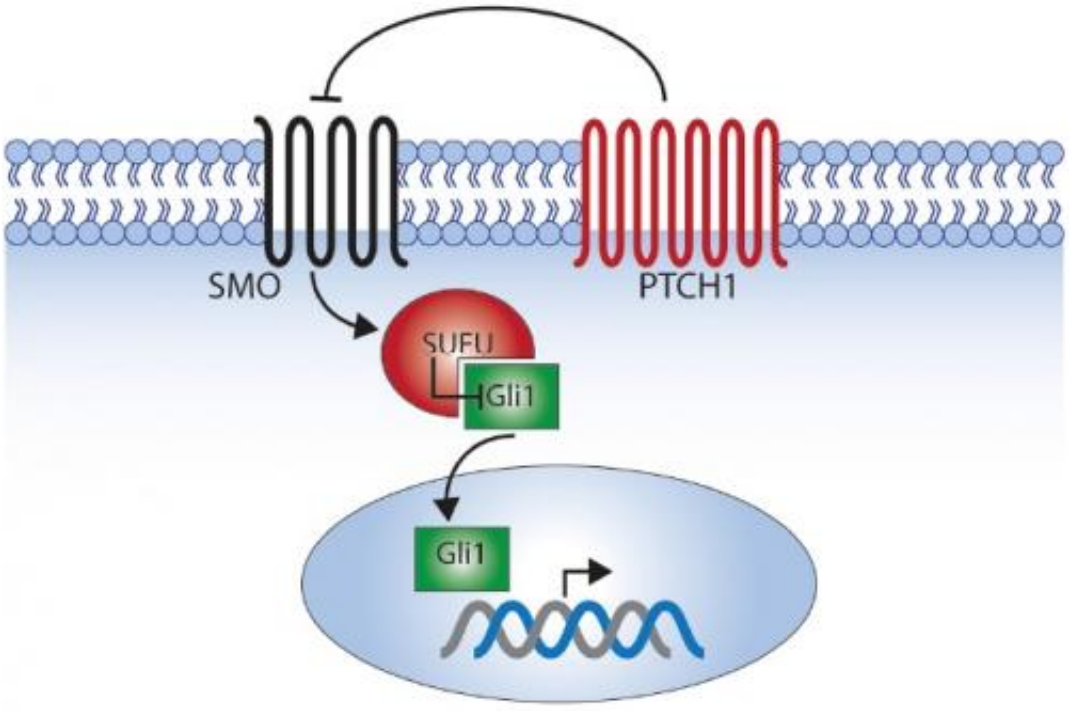

Hedgehog pathway with known cancer genes mutated in this series indicated.

(Medical Xpress)—For the first time, researchers from The Wellcome Trust Sanger Institute, the Royal National Orthopaedic Hospital and UCL Cancer Institute, have linked a gene central to the production of cartilage, COL2A1, to the development of a common type of bone cancer. Their discovery may act as an important way to diagnose this type of cancer in the future, improving patient care.

The team also uncovered the Indian Hedgehog pathway that contributes to the development of this bone cancer in one in five patients with the disease. Drugs that inhibit this pathway already exist, and therefore the team's finding offers potential new treatment options for many patients with this cancer type.

Chondrosarcoma is a cancer of cartilage and is the second most common type of primary bone cancer. The main treatment option is surgery as chemotherapy or traditional radiotherapy provides no significant benefit for patients with this disease. This study offers new approaches to diagnosing this tumour and possible new treatments.

"We've looked at the entire genetic landscape of this bone cancer in patients," says Dr Patrick Tarpey, joint-first author from the Wellcome Trust Sanger Institute. "Our study highlights the importance of thoroughly characterising all cancer types to help develop better therapeutic and diagnostic strategies."

The team screened the functioning regions of the genome in 49 patients with chondrosarcoma. They found that mutations in the gene COL2A1 played a role in cancer development in almost 40 per cent of the patients.

COL2A1 is the gene for a type of collagen. Collagens are fibrous proteins that are responsible for the tensile strength of bone, cartilage and other tissues. This collagen is particularly important for the development of cartilage and thus the gene is very active in cartilage cells. This is the first time that a collagen gene has been shown to be involved in the development of a cancer. The team speculates that the high activity of COL2A1 in cartilage cells could contribute to the formation of mutations that underlie the development of chondrosarcoma.

The team looked at the activity of COL2A1 in other bone cancers but did not find mutations. The high frequency of mutation in COL2A1 in chondrosarcoma patients could therefore become a diagnostic marker to differentiate it from other bone cancers.

"The frequency and pattern of COL2A1 mutations is very interesting," says Dr Sam Behjati, joint-first author from the Wellcome Trust Sanger Institute. "These patterns suggest selection for variants likely to impair normal collagen biosynthesis."

The team also identified two biological pathways, IHH and RB1 that contributes to the development of chondrosarcoma in many patients. Drugs that target the IHH pathway are already used to treat other cancer types. These drugs could be good candidate treatments for patients with chondrosarcoma.

"Our study has brought us a step closer to understanding fully the biological mechanisms that underlie this bone cancer," says Dr Andy Futreal, senior author and honorary WTSI faculty member now at MD Anderson. "This is significant progress that hopefully will lead to more effective approaches to treat this disease."

"Our research would not have been possible without the help of the patients who donated their samples," says Professor Adrienne Flanagan, lead author from the Royal National Orthopaedic Hospital NHS Trust and UCL. "We hope the ongoing scientific and clinical research being conducted will help improve the outlook for those currently suffering at the hands of this disease."

More information: Tarpey, P. et al. Frequent mutation of the major cartilage collagen gene, COL2A1, in chondrosarcoma, *Nature Genetics*, 2013. DOI: 10.1038/ng.2668

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