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News Release

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Gene study pinpoints process that triggers painful bone disease

Scientists have pinpointed the mechanism by which a key gene contributes to the development of a painful bone disease.

Researchers have found that a fault in the gene can trigger the bone defects that affect people with Paget's disease, a condition that leads to bone pain, bone deformity and arthritis. The disease affects up to one million people in the UK.

The team is the first to identify that the gene – called OPTN – regulates the activity of specialised cells that keep bones healthy by breaking down old bone and replacing it.

In Paget's disease the number and activity of these bone-removing cells – called osteoclasts – are increased. This leads to the formation of abnormal bone and development of the disease.

In a study published in the journal *Cell Reports*, scientists from the University of Edinburgh have identified the novel role played by OPTN in bone metabolism.

The researchers have shown that OPTN regulates bone maintenance by slowing down the formation of bone-removing cells to keep the process of bone-removing and bone-building in balance.

The study identifies that genetic variations that increase the risk of disease do so by reducing the amount of OPTN produced by cells.

This, in turn, leads to an increase in the number of bone-removing cells, prompting the normal repair process to go into overdrive and causing bones to become deformed and enlarged.

The researchers found that the gene is frequently less active in people with increased susceptibility to the disease. Further study found that mice with a defective version of the gene are more prone to the disease.

Edinburgh scientists have previously found that genetic variations in OPTN increase the risk of developing Paget's disease, but its role in bone maintenance was unknown until now.

The latest research is a collaboration between the Universities of Edinburgh and Dundee.

Lead researcher Dr Omar Albagha, of the University of Edinburgh's Institute of Genetics and Molecular Medicine, said: "This study advances our understanding of disease mechanisms and identifies a novel molecular pathway that could form a target for new therapeutic treatment for this painful condition."

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