

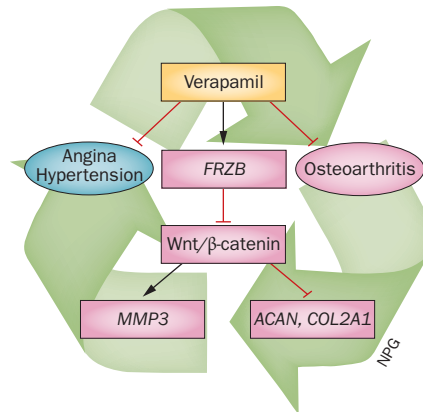
## OSTEOARTHRITIS

# Repositioning verapamil—for Wnt of an OA treatment

'Recycling' drugs could save time and money by allowing those already tested for dose, contraindications and the occurrence of adverse events in the treatment of one disease to be fast-tracked for clinical application to combat other diseases for which we need new medicines, such as osteoarthritis (OA).

Kinji Ohno, the corresponding author of a 'drug-repositioning' study now published in *PLoS ONE* says "we identified that a commonly used calcium-channel blocker, verapamil, efficiently ameliorates OA in a rat model and is a potential therapeutic agent that can be readily applied in clinical practice."

Ohno's team in Nagoya, Japan, scanned available FDA-approved medications and came up with a short-list of 41 drugs that can drive expression of *FRZB* and thereby inhibit Wnt/ $\beta$ -catenin signalling, a pathway that Ohno says can "induce hypertrophic differentiation of chondrocytes and is abnormally activated in OA."



Verapamil a class IV antiarrhythmic agent approved in 1982 by the FDA for the treatment of complications of cardiovascular disease, such as angina and hypertension, was found to be the most powerful dose-dependent activator of *FRZB* expression in human OA chondrocytes. Seven other calcium-channel blockers were also tested, but none had an effect on *FRZB* expression or Wnt/ $\beta$ -catenin signalling.

Verapamil regulated the expression of Wnt-signalling genes, including *ACAN*, *COL2A1* and *MMP3*, and intra-articular injection of the drug inhibited progression of disease in a rat model of OA (destabilization of the medial meniscus).

Rik Lories, an expert in Wnt signalling pathways in cartilage and bone, says "drugs with cartilage protective effects are still largely lacking and this study may have long-term beneficial consequences for OA patients."

Ohno has also applied similar drug repositioning strategies to other diseases. He "found at least one effective drug in each disease model," and he says "five additional screening projects are currently underway."

Nicholas J. Bernard

**Original article** Takamatsu, A. *et al.* Verapamil protects against cartilage degradation in osteoarthritis by inhibiting Wnt/ $\beta$ -catenin signaling. *PLoS ONE* doi:10.1371/journal.pone.0092699