New orally available drug for spinal cord injury found to be safe and tolerable in healthy participants

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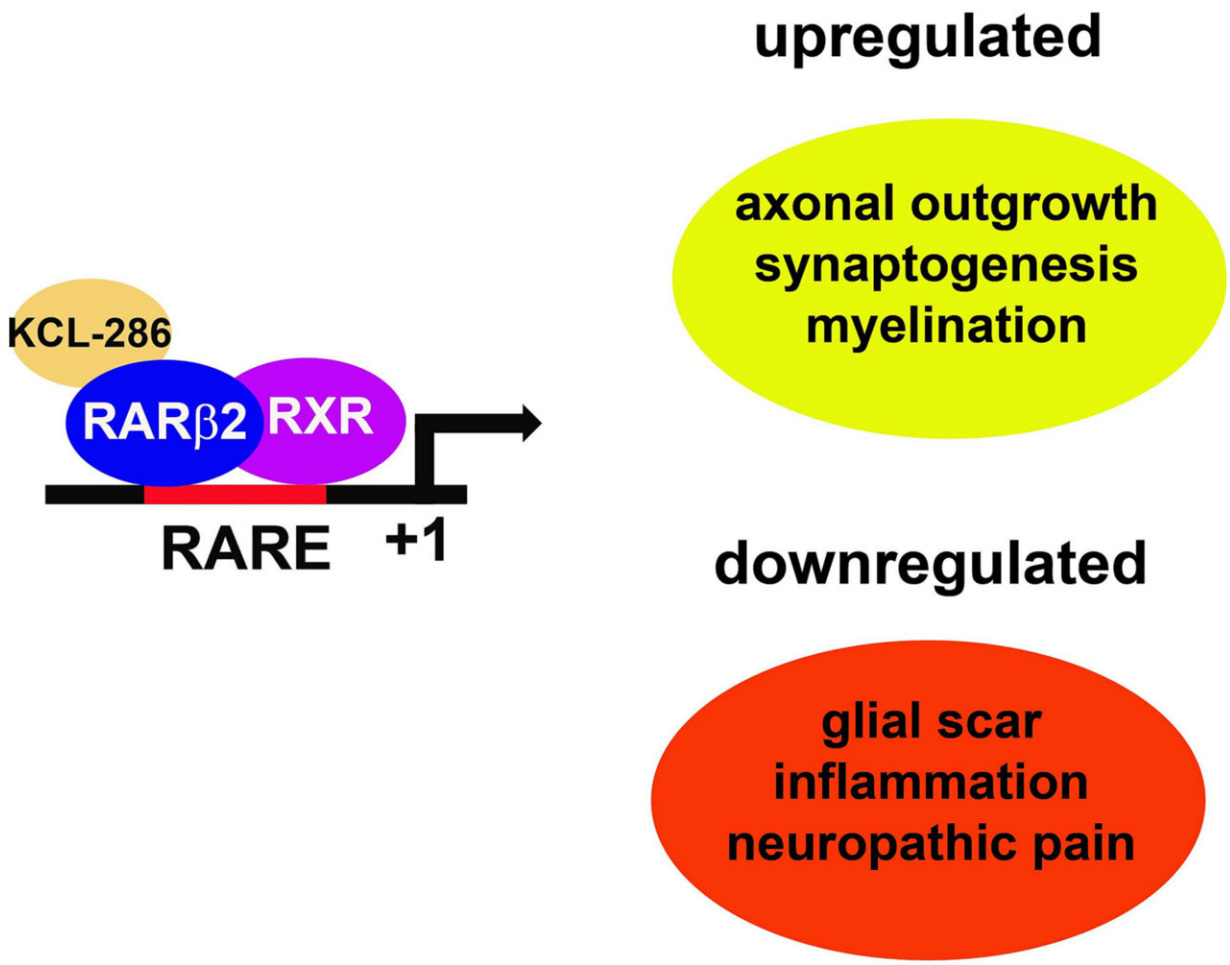

KCL-286 transcriptional neuronal signaling. KCL-286 binds to a retinoic acid receptor (RAR)β2/retinoid x receptor (RXR) heterodimer located at a retinoic acid response element (RARE). This results in activation of transcriptional

pathways required for axonal regeneration. Credit: *British Journal of Clinical Pharmacology* (2023). DOI: 10.1111/bcp.15854

New orally available drug for spinal cord injury found to be safe and tolerable in healthy participants

New research from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at King's College London has demonstrated the safety and tolerability of a new drug treatment designed as a therapeutic intervention for spinal cord injury (SCI).

The research, published in *British Journal of Clinical Pharmacology*, found that the *KCL-286* drug—which works by activating retinoic acid receptor beta (RARb) in the spine to promote recovery—was well tolerated by participants in a Phase 1 clinical trial, with no severe side effects. Researchers are now seeking funding for a Phase 2a trial studying the safety and tolerability of the drug in those with SCI.

Global prevalence of SCI is estimated to be between 0.7 and 1.2 million cases per year, with falls and road accidents being the major causes. Despite incurring a cost of $4 billion per year in direct health care and indirect costs (i.e. inability to work and social care) in the US alone, there are no licensed drugs that can tackle the intrinsic failure of the adult central nervous system to regenerate, and thus remains a largely unmet clinical need.

Previous research by various groups has shown that nerve growth can be stimulated by activating the RARb2 receptor, but no drug suitable for humans has been developed. KCL-286, an RARb2 agonist[1], was developed by Professor Corcoran and team and used in a first in man study to test its safety in humans.

109 healthy males were divided into one of two trial groups; single ascending dose (SAD) adaptive design with a food interaction (FI) arm, and multiple ascending dose (MAD) arm. Participants in each arm were further divided into different dose treatments.

SAD studies are designed to establish the safe dosage range of a medicine by providing participants with small doses before gradually increasing the dose provided. Researchers look for any side effects, and measure how the medicine is processed within the body. MAD studies explore how the body interacts with repeated administration of the drug, and investigate the potential for a drug to accumulate within the body.

Researchers found that participants were able to safely take 100mg doses of KCL-286, with no severe adverse events.

Professor Jonathan Corcoran, Professor of Neuroscience and Director of the Neuroscience Drug Discovery Unit, at King's IoPPN and the study's senior author said, "This represents an important first step in demonstrating the viability of KCL-286 in treating spinal cord injuries. This first-in-human study has shown that a 100mg dose delivered via a pill can be safely taken by humans. Furthermore, we have also shown evidence that it engages with the correct receptor."

"Our focus can hopefully now turn to researching the effects of this intervention in people with spinal cord injuries."

Dr. Bia Goncalves, a senior scientist and project manager of the study, and the study's first author from King's IoPPN said, "Spinal Cord Injuries are a life changing condition that can have a huge impact on a person's ability to carry out the most basic of tasks, and the knock-on effects on their physical and mental health are significant."

"The outcomes of this study demonstrate the potential for therapeutic

interventions for SCI, and I am hopeful for what our future research will find."

More information: Maria B. Goncalves et al, Phase 1 safety, tolerability, pharmacokinetics and pharmacodynamic results of KCL-286, a novel retinoic acid receptor-β agonist for treatment of spinal cord injury, in male healthy participants, *British Journal of Clinical Pharmacology* (2023). DOI: 10.1111/bcp.15854

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