# REGIONAL CENTRE FOR BIOTECHNOLOGY

## Journal Club

## "TRPV1 Pain Receptors Regulate Longevity and Metabolism by Neuropeptide Signaling"

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**ATPC Seminar room**

# Abstract

The sensation of pain is associated with increased mortality, but it is unknown whether pain perception can directly affect aging. We find that mice lacking TRPV1 pain receptors are long-lived, displaying a youthful metabolic profile at old age. Loss of TRPV1 inactivates a calcium-signaling cascade that ends in the nuclear exclusion of the CREB-regulated transcriptional coactivator CRTC1 within pain sensory neurons originating from the spinal cord. In long-lived TRPV1 knockout mice, CRTC1 nuclear exclusion decreases production of the neuropeptide CGRP from sensory endings innervating the pancreatic islets, subsequently promoting insulin secretion and metabolic health. In contrast, CGRP homeostasis is disrupted with age in wild-type mice, resulting in metabolic decline. We show that pharmacologic inactivation of CGRP receptors in old wildtype animals can restore metabolic health. These data suggest that ablation of select pain sensory receptors or the inhibition of CGRP are associated with increased metabolic health and control longevity.