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# THE ROLE OF RET-GFL SIGNALING ON BLADDER SENSATION

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Visceral pain conditions such as interstitial cystitis/painful bladder syndrome (IC/PBS) affect nearly one million U.S. adults, and present a significant depression in quality of life for these patients. Treatment options for IC/PBS are limited and often ineffective, due in part to the preferential study of pain in the somatic system. One pathway that has a demonstrated role in the modulation of pain is the RET-GFL neurotrophic signaling pathway. RET is the co-receptor for the GDNF family of ligands (GFLs), a group of neurotrophic factors with functional roles in renal development, enervation of the gastrointestinal tract, and neural growth and survival. Notably, GFLs have been shown to reverse neuropathic pain when supplied exogenously to damaged sensory neurons and prevent the establishment of neuropathic pain; RET-GFL signaling has also been shown to modulate somatic sensation. However, the role of RET-GFL signaling on visceral sensation has yet to be firmly established. Our aim was to characterize the effect of endogenous RET-GFL signaling on bladder sensation. We found that attenuation of RET-GFL signaling decreases the visceromotor response to noxious bladder distension *in vivo*. *In vitro*, bladder afferents that express RET were more likely to respond to capsaicin, the agonist for TRPV1, a channel implicated in bladder pain, than bladder afferents that do not express RET. Furthermore, there is a trend that bladder afferents expressing RET have higher peak responses to capsaicin than bladder afferents that do not express RET. Finally, afferents expressing RET are significantly more likely to respond to mustard oil, the agonist for TRPA1, a channel also implicated in bladder pain, than afferents not expressing RET. This data taken together suggests that the RET-GFL pathway may be a plausible therapeutic target for IC/PBS and other visceral pain conditions.