CHRONIC PAIN CONDITIONS DRAMATICALLY TRANSFORM THE SOMATOSENSORY NERVOUS SYSTEM, FROM ONE IN WHICH PAIN SERVES AS A WARNING SIGNAL, PROMOTING LIFE AND SURVIVAL, TO ONE IN WHICH PAIN IS EVOKED BY EVERYDAY ACTIVITIES, WHICH GREATLY REDUCES QUALITY OF LIFE. WE INVESTIGATE THIS ALTERED SENSORY PROCESSING OR ‘PLASTICITY’ THAT OCCURS IN CHRONIC PAIN CONDITIONS, WITH THE AIM OF IDENTIFYING NOVEL THERAPIES.

CHRONIC PAIN CONDITIONS
Chronic pain conditions arise following tissue damage or injury to the peripheral and or central nervous system and are broadly termed ‘inflammatory’ or ‘neuropathic’, respectively. Both inflammatory and neuropathic pain conditions are characterised by spontaneous pain, hyperalgesia (exacerbated pain) and allodynia (touch-evoked pain) (Fig 1). In the case of inflammatory pain, these symptoms may play a role in repair, promoting recovery by limiting contact with, for example wounded tissue. However, if these symptoms persist beyond tissue healing, or in the case of neuropathic conditions exist without any peripheral tissue damage, these chronic pain symptoms can be extremely unpleasant and debilitating.

Treatment options for these painful conditions are frequently ineffective or are limited by adverse side effects. A greater understanding of the mechanisms underlying the abnormal processing of sensory information in chronic pain conditions is required to identify novel therapeutic targets, and this is our main research focus.

SENSORY PLASTICITY
In chronic pain conditions a multitude of molecular and cellular changes occur within both peripheral and central sensory pathways and these are thought to underlie the misprocessing of sensory information that results in chronic pain sensation. Crucial to understanding chronic pain must therefore be the functional study of the neuronal networks that actually translate these underlying molecular and cellular changes into chronic pain sensation. The wiring of the somatosensory nervous system is complex, and until recently it has been difficult to study the function of specific components of the circuitry. The development of transgenic and related approaches to fluorescently pre-identify specific neuronal subtypes (Fig 2) has however revolutionized our ability to study the function of defined sensory circuits. Using this fluorescent pre-identification approach, we aim to identify...
plasticity in chronic pain conditions, with the goal of then targeting treatment selectively to the affected circuits, thereby reducing deleterious side effects.

**SPINAL OUTPUT NEURONS**

Sensory information is conveyed by peripheral sensory nerve fibres to the dorsal horn of the spinal cord, which is the first stage of central processing of sensory input. The processing of sensory information within the dorsal horn is complex, involving local excitatory and inhibitory influences, as well as descending modulation from the brain. Importantly, this dorsal horn sensory processing crucially determines which sensory signals are sent to higher centres to be perceived, where they may also influence emotional and autonomic function.

Our major interest is a group of spinal cord output neurons that relay pain signals to the brain and have been shown to be critically required for chronic pain. Because these output neurons can be visualized using fluorescence, in the spinal cord slice preparation, it is possible to directly study the activity of these output neurons using in vitro patch clamp electrophysiology. I have previously shown that these key output neurons normally only respond to ‘nociceptive’ sensory input but when local spinal inhibitory control is disrupted (mimicked pharmacologically) as occurs in chronic pain conditions, they now show a completely novel response to innocuous sensory input (Fig 3). This is a potential basis for the debilitating symptom of allodynia when chronic pain patients experience pain sensation to non-painful stimuli such as touch.

Chronic pain conditions however, involve a vast array of changes which cannot simply be mimicked in vitro. Using similar electrophysiological approaches we are currently characterizing altered sensory processing or ‘plasticity’ in these key output neurons in chronic pain conditions. Investigation of the underlying plasticity mechanisms will aid in identifying targets to minimize sensory misprocessing and thereby reduce debilitating chronic pain.

![Figure 2](image2.png)

**Figure 2.** Overlay showing GFP-immunoreactivity (green) and NeuN-immunoreactivity (red) in spinal cord dorsal horn of a Pde1c-GFP BAC transgenic mouse. NeuN is a reliable marker of all spinal cord neurons. Pde1c-GFP neurons are present in ‘pain’ regions of the spinal cord dorsal horn. The insets (bottom left) show higher magnification images of the boxed area shown at right. Arrows show examples of double labeled profiles. Scale bar, 100μm

![Figure 3](image3.png)

**Figure 3.** Schematic illustrating spinal cord circuits that may be important for chronic pain

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**Selected References**


Torsney C and MacDermott AB. Disinhibition opens the gate to pathological pain signaling in superficial neurokinin 1 receptor-expressing neurons in rat spinal cord. J Neurosci 2006 Feb 8:26(6):1833-43.


Torsney C and Fitzgerald M. Age-dependent effects of peripheral inflammation upon the electrophysiological properties of neonatal rat dorsal horn neurons. J Neurophysiol 87(3):1311-7, 2002

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