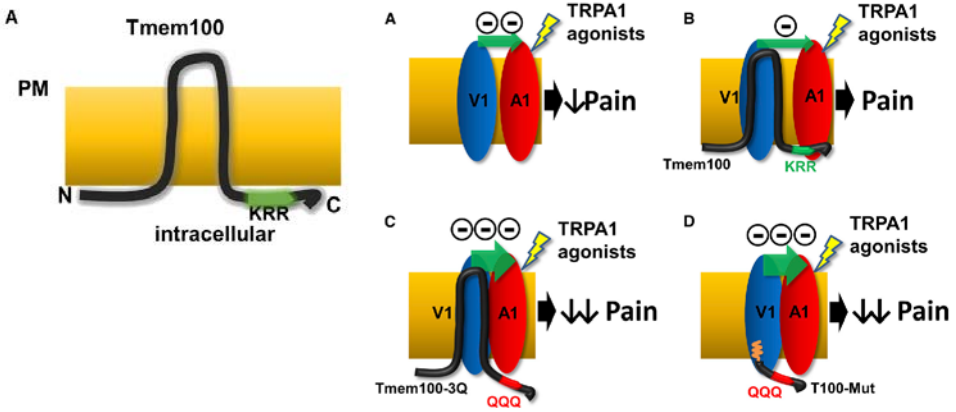
Meeting of the Interagency Pain Research Coordinating Committee

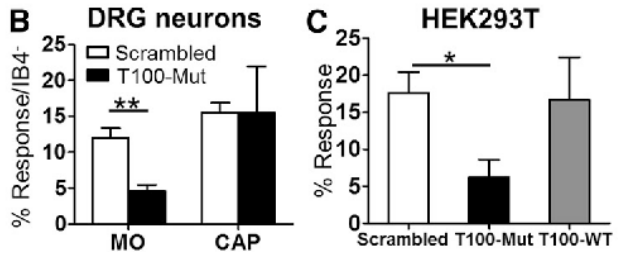
December 3rd, 2015

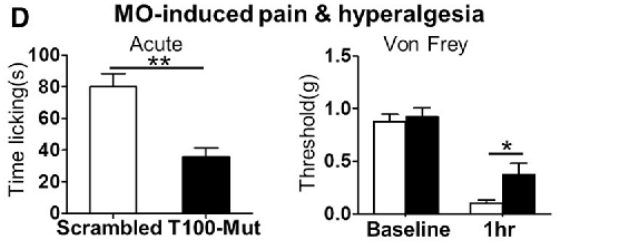
Porter Building, Rm 610
NIH Main Campus

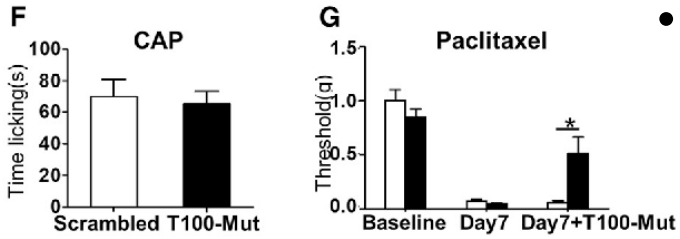
Tmem100: A novel pain modulator, and potential therapeutic target



- TRPV1 and TRPA1 are key pain transducers
- *In vivo*, Tmem100 loosens the physical association between TRPV1 and TRPA1, allowing greater TRPA1 responsiveness and increased pain





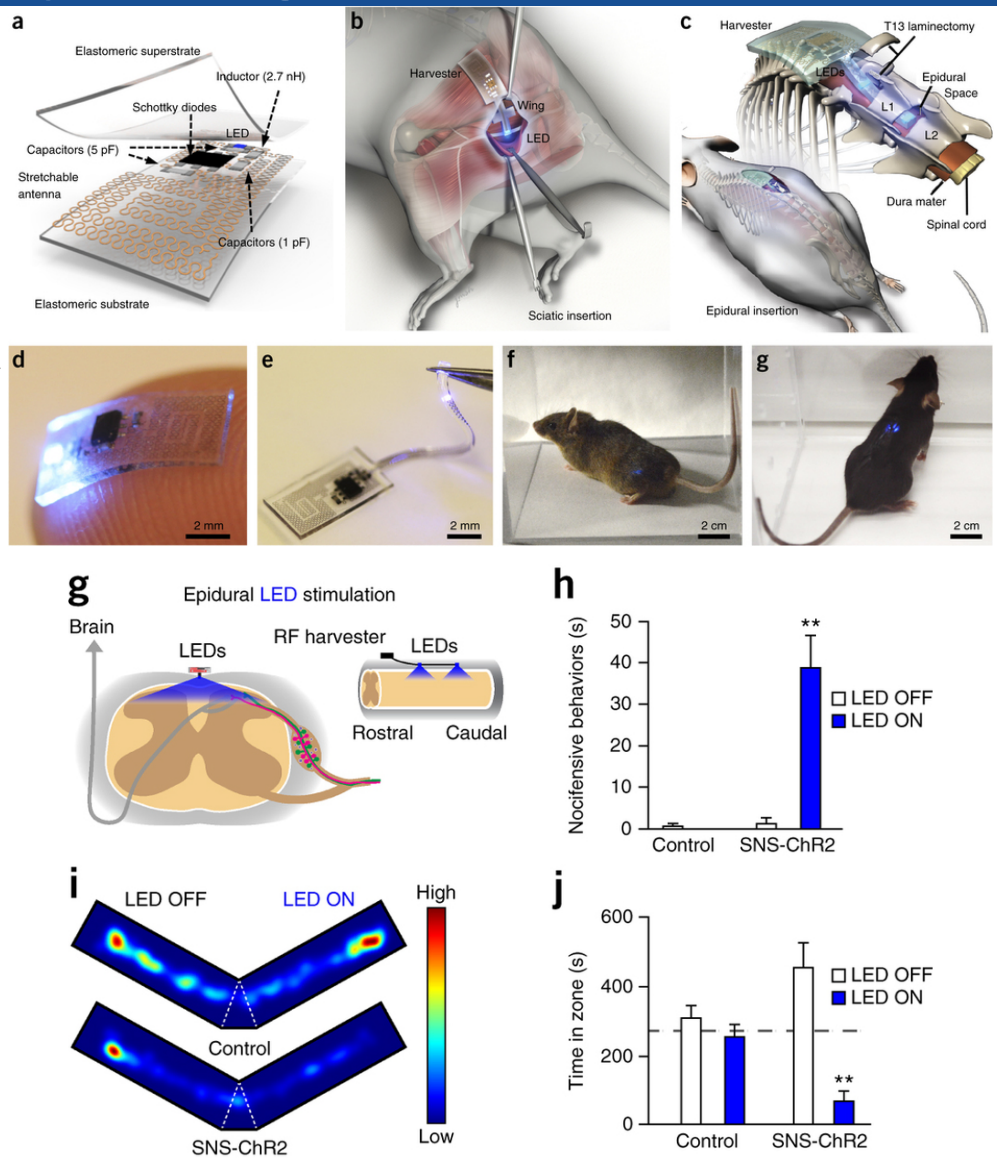


- Mutating the C terminus of Tmem100 tightens the association between TRPV1 and TRPA1, decreasing TRPA1 responsiveness
- Tmem100−/− animals show reductions in pain behavior following inflammatory injury
- Injection of a peptide consisting of the mutated C terminus of Tmem100 partially relieves pain behaviors in an animal model
- Tmem100 is a strong viable target for the alleviation of acute mechanical pain

Weng *et al*. **Neuron** Feb 2015

Implantable wireless devices can control pain signals

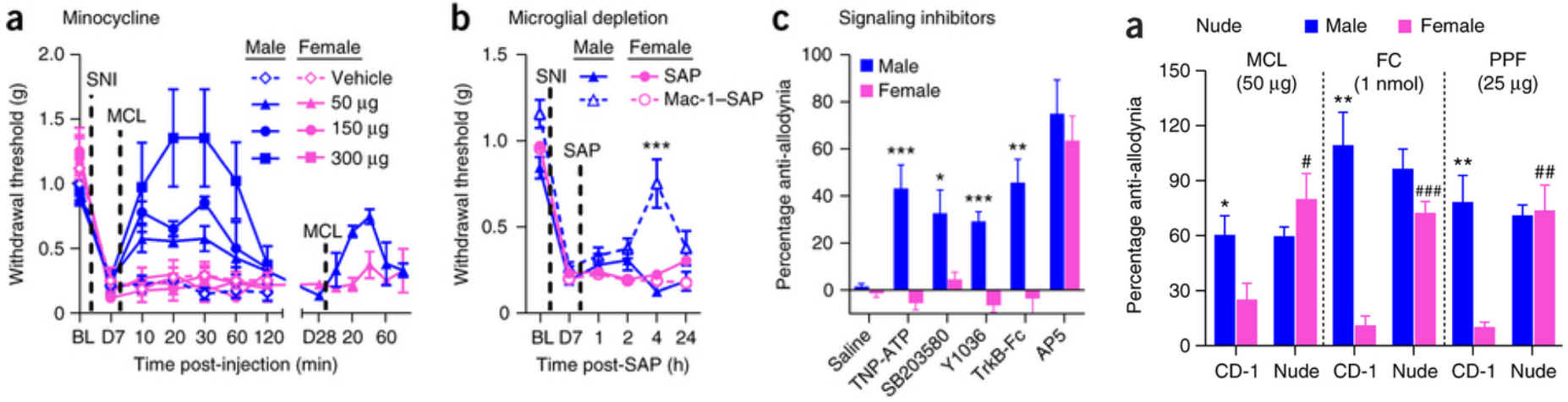
- Optogenetics allows rapid, temporally specific control of neuronal activity by targeted expression and activation of light-sensitive proteins in neurons
- This paper represents a technological leap in developing soft, stretchable, fully implantable miniaturized systems for wireless optogenetics
- Wireless activation of channelrhodopsin-2 expressed in nociceptive pathways resulted in spontaneous pain behaviors and place aversion
- These implantable devices can activate — and, in theory, block — pain signals in the peripheral nervous system before those signals reach the brain



Park *et al*. **Nature Biotechnology** Nov 2015

Sexual dimorphism in microglial contribution to pain

- Basic science research clearly shows that microglia-to-neuron signaling is essential for chronic pain hypersensitivity – but most of these studies have used male animals
- However, many pain conditions are more common in women than men
- This study examined whether sex affects microglial involvement in nerve injury pain
- The authors found that microglia are not required for nerve injury-induced mechanical pain in female mice
- Adaptive immune cells (T cells) are key instead
- Distinct strategies targeting neuroimmune signaling may be required for the treatment of chronic pain in men versus women



Sorge *et al*. **Nature Neuroscience** Aug 2015

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

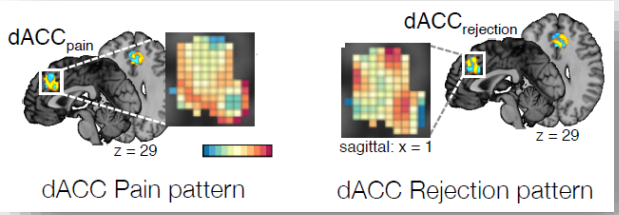
FORUM ON NEUROSCIENCE AND NERVOUS SYSTEM DISORDERS
Board on Health Sciences Policy

November 10, 2015

Institute of Medicine

*Explore the application of the **Accelerating Medicines Partnership** (AMP) approach to **pain**. Discuss challenges and identify what would be needed to make this therapeutic domain a good candidate for this approach.*

- **Biomarker Development**
  - Brain Imaging
  - Peripheral biomarkers



Tor Wager, 2015 presentation

- **Use of Data Registries**

Collaborative Health Outcomes Information Registry (CHOIR)

CHOIR Collaborative Health Outcomes Information Registry

Sean Mackey, 2015 presentation

Discussion of AMP for Pain

Topics discussed:

- Development of biomarkers for pain
- Identifying responders v. non-responders to minimize risk of clinical trial failure
- Understanding/circumventing the 'placebo effect' in clinical trials
- Considering pain duration as a target with the goal of reducing the duration of acute pain as well as the transition to chronic pain
- IPRCC – Use of Federal Pain Research Strategy to identify potential research areas that are ideal for an AMP