Microscopy TODAY

Coming Events

2020

APMC-2020 – 12th Asia-Pacific Microscopy Conference
February 3–7, 2020
Hyderabad, India
www.apmc12.in

Biophysical Society 64th Annual Meeting
February 15–19, 2020
San Diego, CA
www.biophysics.org/Meetings/AnnualMeeting/FutureAnnualMeetings/tabid/495/Default.aspx

ACMM 26 – 26th Australian Conference on Microscopy and Microanalysis
February 16–20, 2020
Canberra, Australia
www.acmm26.org/welcome

United States and Canadian Academy of Pathology (USCAP) Annual Meeting 2020
February 29–March 5, 2020
Los Angeles, CA
www.uscap.org/uscap-annual-meeting

15th European Molecular Imaging Meeting – EMIM 2020
March 24–27, 2020
Thessaloniki, Greece
www.e-smi.eu/index.php?id=1976

FOM2020 – Focus on Microscopy
April 5–8, 2020
Osaka, Japan
http://focusonmicroscopy.org

Microscopy & Microanalysis 2020
August 2–6, 2020
Milwaukee, WI
www.microscopy.org

2021

Microscopy & Microanalysis 2021
August 1–5, 2021
Pittsburgh, PA
www.microscopy.org

2022

Microscopy & Microanalysis 2022
July 31–August 4, 2022
Portland, OR
www.microscopy.org

2023

Microscopy & Microanalysis 2023
July 24–28, 2023
Minneapolis, MN
www.microscopy.org

2024

Microscopy & Microanalysis 2024
July 28–August 1, 2024
Cleveland, OH
www.microscopy.org

Carmichael's Concise Review

A New Organ for Feeling Pain

Stephen W. Carmichael
Mayo Clinic, Rochester, MN 55905

carmichael.stephen@mayo.edu

Perceiving pain is essential to survival of an organism. One definition of pain is the perception of harmful stimuli. This may be from an internal (inflammation, bowel distention, etc.) or external stimulus (for example, mechanical or thermal), and these types of pain are perceived by nociceptive pain receptors. The current view is that external harmful (noxious) stimuli directly activate unmyelinated nerve endings in the skin. These nerve endings are associated with Remak glial cells that protect and metabolically support the unmyelinated nerves. These Remak glial cells are Schwann cells that do not myelinate the axons. Recently Hind Abdo, Laura Calvo-Enrique, Patrik Ernfors, and others investigated how these cutaneous Remak Schwann cells are distributed and interact with receptors (nociceptive nerve terminals) for detection of noxious stimuli [1]. What they found is described as a distinct type of Schwann cell and a new organ for feeling pain.

Abdo et al. used genetic labeling to identify these cutaneous Schwann cells. Recombination of specifically tagged cells revealed their location in the dermis near the border with the epidermis (Figure 1). Combining this with specific stains for neurons demonstrated that epidermal Schwann cell processes attached to the nerves. Transmission electron microscopy showed that nerve terminals emerged from the soma of Schwann cells located a few micrometers from the border of the epidermis and that the glial cell was the only source of cytoplasmic sheaths for the nerve terminals. These morphologically distinct glia also had other vital characterisitics such as a high expression of aquaporin, a protein that functions in water balance of cells. Nerve and Schwann cell processes were surrounded by a thick layer of fibrillar collagen that was distinct from the rest of the collagen in the dermis. Immunoelectron microscopy further confirmed the existence of a morphologically and molecularly specialized type of Schwann cell that formed a mesh-like network in the subepidermal border. This constituted a glial-neural complex with an intimate association with nociceptive nerves, which is insulated by a structural support of collagen fibers. Abdo et al. called these specialized glial cells nociceptive Schwann cells. These nociceptive cells were found to be a population distinct from other cutaneous Schwann cells.

After the nociceptive Schwann cells were clearly identified, Abdo et al. used a technique called optogenetics to determine if these cells could be stimulated by painful stimuli. Since these cells are located superficially, intense light stimulation was used and was found to elicit limb withdrawal in certain strains of mice. This withdrawal

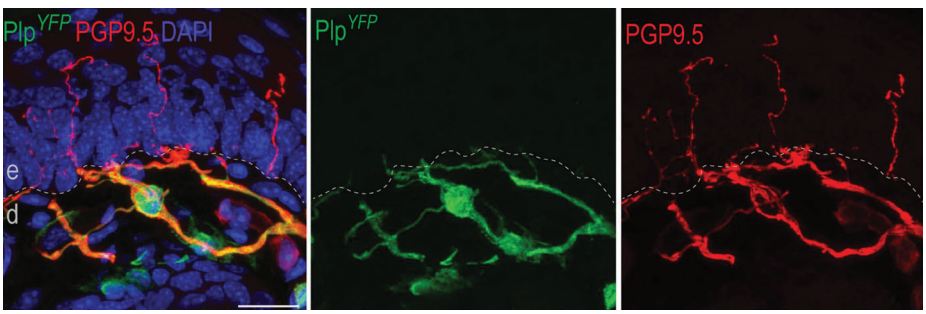

Figure 1: Genetically expressed myelin proteolipid protein, indicated by the marker protein gene product 9.5, and yellow fluorescent protein. Nociceptive Schwann cells in the sub-epidermal border ensheathed unmyelinated nerve endings in mice. Scale bar is 10 μm.

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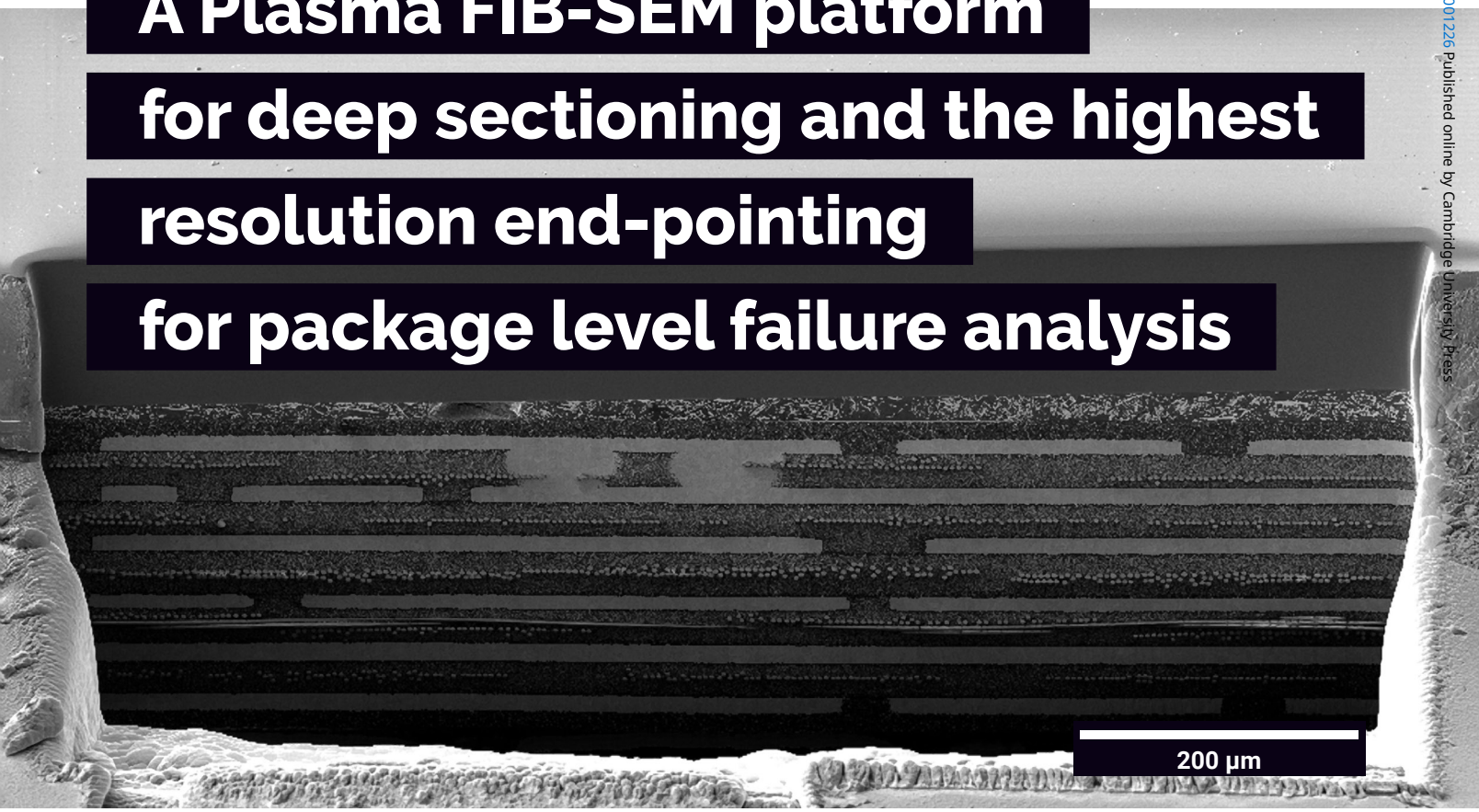

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also elicited shaking and licking of the paw, which are considered to be pain-specific behaviors, and was associated with increased electrical activity in nerves from the paw.

Electrical properties of nociceptive Schwann cells in response to mechanical stimuli were also examined in cultured cells by whole-cell current-clamp electrophysiological recordings. It was found that nociceptive Schwann cells responded to both positive and negative changes in force but much less to sustained force. This and other evidence suggests a very fast response of these cells to mechanical stimuli, similar to what has been described in sensory neurons.

Abdo et al. provide strong evidence for a specialized glial cell type that forms a newly described sensory organ in the skin, responsible for initiating the sensation of pain. The nociceptive Schwann cells and nociceptive nerves form a pain-detecting glial-neural complex with two sensor-receptor cell types: the glia and the nerve. The functional implications of these findings are immense, presenting a new way that animals perceive pain. This is not only important for a better understanding of how the body performs this essential perception of pain, but it could play a key role in developing future therapies for dealing with pain, including treatment of debilitating clinical conditions such as chronic pain syndromes.

References

[1] Abdo et al., *Science* 365 (2019) 695–99.

[2] The author gratefully acknowledges Dr. Patrik Ernfors for reviewing this article.

MT

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Complete course descriptions and registration form will be online in October 2019 at **lehigh.edu/microscopy**

For more information contact Nikki Rump at nikki.rump@lehigh.edu or call 610.758.1112