

Distinguished Lecture Series in Physiology

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**“Dietary fatty acids fine-tune
neuronal and non-neuronal
cells mechanical response”**

Mechanosensitive ion channels rely on membrane composition to transduce physical stimuli into electrical signals. The Piezo1 channel mediates mechanoelectrical transduction and regulates crucial physiological processes, including vascular architecture and remodeling, cell migration, and erythrocyte volume. Whereas Piezo2 is essential for touch discrimination, vibration, and proprioception. The identity of the membrane components that modulate Piezo channels function remain largely unknown. Using lipid profiling analyses, we identified dietary fatty acids that tune Piezo channels mechanical response. We found that margaric acid, a saturated fatty acid present in dairy products and fish, inhibits Piezo1 and Piezo2 activation and polyunsaturated fatty acids (PUFAs), present in fish oils, modulate Piezo1 inactivation. Using atomic force microscopy, we revealed that margaric acid increases membrane bending stiffness, whereas PUFAs decrease it. We use PUFA supplementation to abrogate the phenotype of gain-of-function Piezo1 mutations (causing hemolytic anemia), and margaric acid to counteract PIEZO2 sensitization by the proalgesic agent bradykinin. Beyond Piezo channels, our findings demonstrate that cell-intrinsic lipid profile and changes in the fatty acid metabolism can dictate the cell's response to mechanical cues.

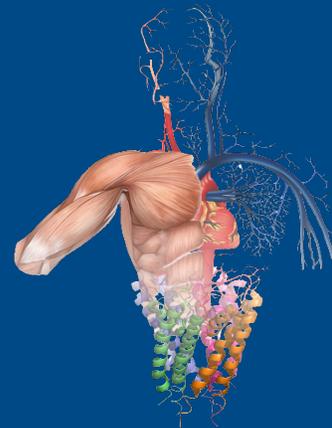
Monday, February 7, 2022
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Zoom

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7



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