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## NSAID Receptor Responsible for Olive Oil's 'Cough' and More

*Combination of sensory and molecular approaches identify receptor sensitive to anti-inflammatory compounds*

PHILADELPHIA (January 18, 2011) – Scientists from the Monell Center and collaborators report that a receptor known as TRPA1 is activated by two structurally unrelated anti-inflammatory compounds. The first, oleocanthal, is a natural polyphenolic anti-inflammatory agent uniquely found in extra virgin olive oil; while the second, ibuprofen, is an over-the-counter non-steroidal anti-inflammatory drug (NSAID).

The researchers also demonstrate that the TRPA1 receptor is spatially localized to the back of the throat, which is exactly where the distinctive irritating sting from olive oil is felt. This unique sensation and the accompanying 'cough' are regarded among connoisseurs as indicators of high quality olive oil.

"We believe that the TRPA1 receptor elicits cough to protect the lungs from chemical insult, for example from toxins in the air," said Paul A.S. Breslin, Ph.D., one of the corresponding authors and a sensory biologist at Monell.

In 2005, Monell researchers and collaborators announced the discovery that oleocanthal is a non-steroidal, anti-inflammatory agent that inhibits activity of cyclooxygenase (COX) enzymes, a pharmacological action shared by ibuprofen.

The finding was based on the sensory observation that olive oil irritates the back of the throat in a highly characteristic manner identical to that experienced with liquid ibuprofen.

At that time, the researchers also demonstrated that oleocanthal caused the irritating throat sting associated with extra virgin olive oils.

The current study, published in the *Journal of Neuroscience*, extends those findings by identifying TRPA1 as the receptor that is activated by both oleocanthal and ibuprofen. Further, the findings establish that oleocanthal causes the distinctive sting of olive oil through its activation of TRPA1. Similarly, activation of the same receptor produces ibuprofen's irritating sensation.

The findings may provide novel insights into anti-inflammatory pharmacology. "This receptor may be used to identify other anti-inflammatory compounds that, like ibuprofen and oleocanthal, help prevent major lethal disease," said Breslin.

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“Additionally, since we know how to inhibit this receptor, it may be possible to develop liquid anti-inflammatory medicines that are less aversive. This would especially benefit children, who are unable to swallow pills.”

The study’s combination of sensory, chemical, and molecular approaches may lend insight into other aspects of inflammation and disease.

“Oleocanthal and ibuprofen are chemically unrelated, yet both are potent anti-inflammatory compounds that activate the TRPA1 receptor and cause sensory irritation,” said Monell behavioral biologist Gary K. Beauchamp, Ph.D., also a corresponding author. “This points to a possible mechanistic connection between sensory perception, receptor activation, and pharmacology. An understanding of this connection could someday lead to identification of new anti-inflammatory pathways.”

Future work also will explore several paradoxical associations that relate the sensory and health-promoting aspects of oleocanthal and ibuprofen. Lead author Catherine Peyrot des Gachons, Ph.D., a food scientist at Monell, points out that the two anti-inflammatories promote health while also causing irritation and pain. She comments, “These two facts seem antagonistic and excitingly mysterious from a scientific perspective.”

Beauchamp raises a related question, noting that humans have come to appreciate the ‘pain’ from oleocanthal in olive oil, as if there is an inner knowledge that it is advantageous. “How this happens remains a fascinating puzzle,” he says.

Also contributing to the research were Bruce Bryant and Luba Dankulich-Nagrudny of Monell; Amos B. Smith III of Monell and University of Pennsylvania School of Medicine; Kunitoshi Uchida and Makoto Tominaga of Okazaki Institute for Integrative Bioscience and Graduate University for Advanced Studies, Okazaki, Japan; Asako Shima of Okazaki Institute for Integrative Bioscience; Jeffrey B. Sperry of University of Pennsylvania School of Medicine. Dr. Breslin is also faculty at Rutgers University School of Environmental and Biological Sciences.

The study was funded by the National Institutes of Health.

The Monell Chemical Senses Center is an independent nonprofit basic research institute based in Philadelphia, Pennsylvania. Monell advances scientific understanding of the mechanisms and functions of taste and smell to benefit human health and well-being. Using an interdisciplinary approach, scientists collaborate in the programmatic areas of sensation and perception; neuroscience and molecular biology; environmental and occupational health; nutrition and appetite; health and well-being; development, aging and regeneration; and chemical ecology and communication. For more information about Monell, visit [www.monell.org](http://www.monell.org).

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