Microscopy TODAY

Coming Events

2010

Histochemistry 2010
March 21–23, 2010, Woods Hole, MA
www.histochemistry.org

American Chemical Society
March 21–25, 2010, San Francisco, CA
www.acs.org

Focus on Microscopy 2010
March 28–31, 2010, Shanghai, China
www.focusonmicroscopy.org

Experimental Biology 2010
April 24–28, 2010, Anaheim, CA
www.experimentalbiology.org

SPIE Scanning Microscopy 2010
May 17–19, 2010, Monterey, CA
www.spie.org

Electron Backscatter Diffraction Topical Conference
May 24–26, 2010, Madison, WI
www.microbeamanalysis.org/ebsd-2010

Lehigh Microscopy School
June 6–18, 2010, Bethlehem, PA
www.lehigh.edu/microscopy

3-D Electron Microscopy 2010
June 20–25, 2010, Lucca, Italy
www.grc.org

Microscience 2010
June 29–July 1, 2010, London, UK
www.rms.org.uk

ACMM-21
July 11–15, 2010, Brisbane, Australia
www.microscopy.org.au

Microscopy & Microanalysis 2010
August 1–5, 2010, Portland, OR
www.microscopy.org

International Microscopy Congress
September 19–24, 2010, Rio de Janeiro, Brazil
Abstract deadline is April 15, 2010
www.imc17.com

2011

Microscopy & Microanalysis 2011
August 7–11, 2011, Nashville, TN

2012

Microscopy & Microanalysis 2012
July 29–August 2, Phoenix, AZ

2013

Microscopy & Microanalysis 2013
August 4–8, Indianapolis, IN

More Meetings and Courses
Check the complete calendar near the back of this magazine and in the MSA journal *Microscopy and Microanalysis*.

Carmichael's Concise Review

Cilia Not Only Move, but also Have Taste!

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Motile cilia are organelles that contain amazing molecular machines that bend each cilium in a rhythmic and coordinated movement. This allows a liquid film, perhaps with particles embedded within, to move in a specific direction. The classic example is the cilia of the respiratory passages that move a layer of debris-carrying mucus out of the lungs. When this mechanism is not working properly, recurrent pulmonary infections result. The classic example of this is immotile cilia syndrome that results in chronic bronchitis and related problems. However, no sensory function has been assigned to these classic motile cilia until now (although nodal cilia have both mechanical activity and sensory functions). Alok Shah, Yehuda Ben-Shahar, Thomas Moninger, Joel Kline, and Michael Welsh have demonstrated sensory receptors on motile cilia for the first time [2].

Shah, Ben-Shahar et al. hypothesized that a defense of airways would involve detection of danger signals. Therefore they looked for sensory-related genes in microarray expression data from primary cultures of differentiated human airway epithelia. Molecular tests demonstrated the presence of several members of the bitter taste receptor (referred to as T2R) family in these epithelial cells. However, these tests could not indicate where in the cells T2R genes were expressed.

Antibodies are available for several of the T2Rs and Shah, Ben-Shahar et al. used these for immuno-histochemical studies on human airway epithelia because the antibodies could be tagged with fluorescent markers and then specifically bound to T2R receptors. They found that only ciliated epithelial cells expressed these receptors, and these receptors specifically localized in cilia. Cilia could be definitively identified using an antibody to α-tubulin, which is found in the microtubules characteristic of cilia. Using fluorescent tags that emitted different colors demonstrated the co-localization of T2R receptors and cilia, and yet a different colored tag for nuclei emphasized that T2R was not in the interior of the cell (Figure 1). Almost every ciliated cell expressed 4 of the T2Rs tested, but interestingly the distribution was heterogeneous. This was not only true from cell to cell (where some cells were labeled for more than one T2R) but also at different locations along an individual cilium (some at the tip, some at the base).

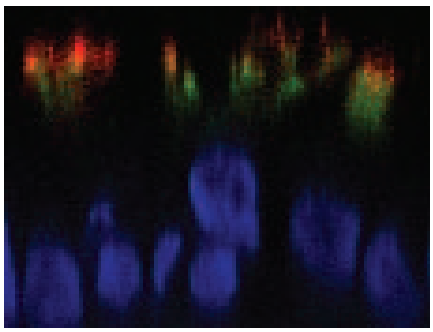

Figure 1: TR2 receptors (green) localize to motile cilia that are identified by tagging a form of tubulin (green). Nuclei are stained blue.

These studies proved the anatomic location of T2R receptors on motile cilia. But what about the functional significance of these receptors? The T2R signal transduction pathway is comprised of several proteins, ultimately affecting the second messenger: the intracellular calcium ion concentration. Some of the proteins of the signal transduction pathway were detected in airway epithelia, and immunohistochemistry demonstrated that they were only present within ciliated cells. To demonstrate that the T2R signaling pathway was functional, Shah, Ben-Shahar et al. applied denatonium, said to be the most bitter compound known to man (used to discourage ingestion of common toxic products such as antifreeze), to human airway epithelia. They found transient, dose-dependent increases in intracellular

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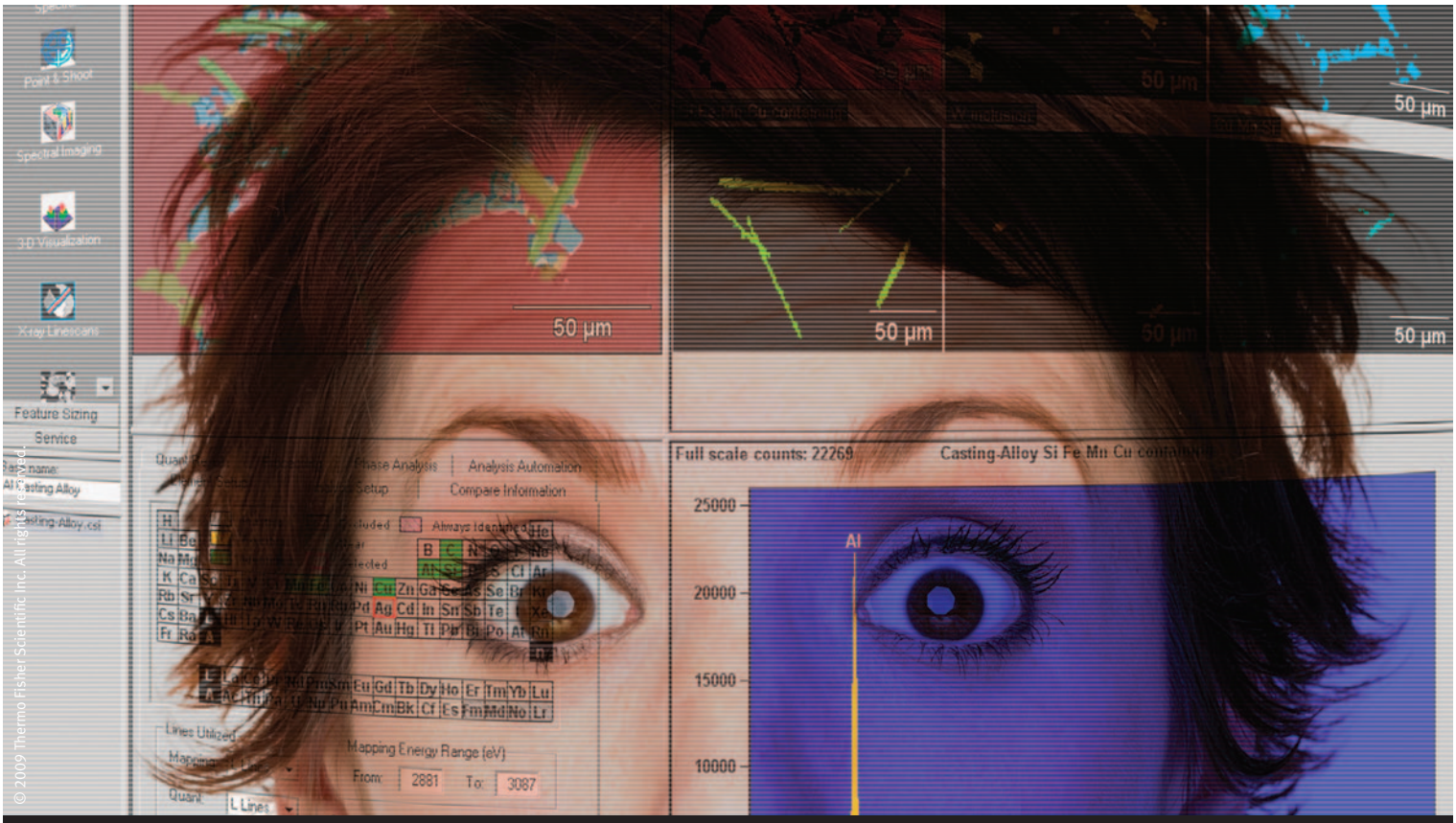

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calcium ion concentrations. This was also true when other bitter compounds, including nicotine, were applied.

When intracellular calcium ion concentrations are increased in one epithelial cell, the effect can rapidly spread through gap junctions to adjacent cells. To test if the ion increase was initiated in ciliated cells, Shah, Ben-Shahar et al. applied bitter compounds directly to the cilia. Calcium ion concentration increased in ciliated cells before being detected in non-ciliated cells, consistent with their finding that the only ciliated cells bear receptors for bitter compounds. Also, the application of bitter compounds was shown to increase ciliary beat frequency by about 25 percent.

These breakthrough findings suggest that control of ciliary activity could at least in part be a local response. Not only could cilia respond to the inhalation of certain compounds, but Shah, Ben-Shahar et al. also suggested that some pathogens could produce compounds that could hasten the expulsion of the pathogen. This is an entirely new concept that could lead to improved treatments for numerous pulmonary diseases!

References

[1] The author gratefully acknowledges Drs. Michael Welsh, Yehuda Ben-Shahar, and Alok Shah for reviewing this article.
[2] AS Shah, Y Ben-Shahar, TO Moninger, JN Kline, and MJ Welsh, *Science* 325 (2009) 1131–34.

MT

Retrograde filling of motor neurons with dextran, tetramethylrhodamine and biotin, 3kDa, lysine fixable ("3kDa micro-ruby"; Molecular Probes [Invitrogen], Eugene, OR) via their axons from the 14th ventral root (14th VR axon). Images generated by Gatan 3View™. Main Image: Image stack composed of 6,000 images demonstrating excellent registration between all images within the image stack. Inset Image: 3kDa micro-ruby labeling and use of DAB allows user to easily contour, segment, and reconstruct type-1 (MN-1) and type-2 motor neurons (MN-2) and the axon of a commissarial primary ascending interneuron (CoPA Axon). Images courtesy of Dr. Eduardo Rosa-Molinar and his group at the University of Puerto Rico-Rio Piedras, San Juan, Puerto Rico.