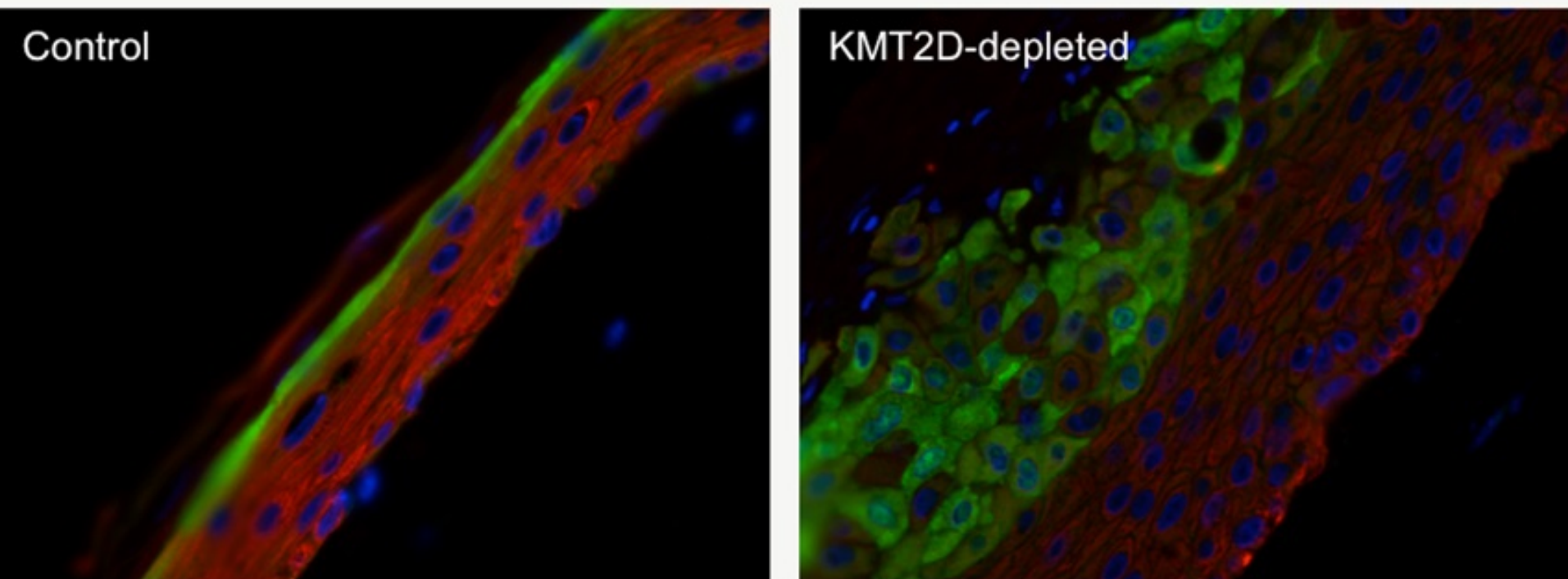


## News Release

# Highly Mutated Protein in Skin Cancer Plays Central Role in Skin Cell Renewal

February 19, 2018



*When KMT2D was depleted (right) from human skin cells, undifferentiated stem cells could not multiply normally, causing different layers of skin epidermis to become thickened and disorganized. Credit: The lab of Brian C. Capell, MD, PhD, Perelman School of Medicine, University Pennsylvania.*

**PHILADELPHIA** – Approximately once a month, our skin completely renews itself. If this highly coordinated process goes awry, it can lead to a variety of skin diseases, ranging from skin cancer to psoriasis. Cells lining such organs as skin and the gut, lungs, and many other organs (collectively called epithelial tissue) rely on a delicate balance of self-renewal, proliferation, and differentiation. However, disruption of this equilibrium may drive cancer and other disorders.

Researchers from the **Perelman School of Medicine at the University Pennsylvania** have shown for the first time that a key protein called KMT2D involved in the epigenetic regulation of gene expression guides this renewal. They published their work this month in *Genes & Development*. Epigenetics involves chemical modifications to DNA and its supporting proteins that affect the availability of genes to be “read” and made into proteins.

“We have known that KMT2D is one of the most frequently mutated genes in all of skin cancer, as well as other epithelial cancers such as those of the lung, esophagus, mouth, and throat,” said senior author **Brian C. Capell, MD, PhD**, an assistant professor of Dermatology and Genetics. “However, prior to this study, we had no idea how those mutations caused cancer or even what KMT2D did in these tissues. Now, armed with this knowledge, I envision in the near future we may be able to test the ability of novel epigenetic drugs to reverse these deleterious mutations.”

In the study, when the researchers depleted KMT2D from human skin cells, undifferentiated stem cells could not multiply normally, causing premature differentiation of the tissue into a more mature, differentiated state. As a result, when grown in three-dimensional cultures, the different layers of skin epidermis became thickened and disorganized.

“Our data suggests that KMT2D is critical for the proper coordination of our skin’s turnover process,” Capell said. “Because epigenetic changes are reversible, we hope that our ongoing studies in KMT2D mouse models will ultimately lead to identifying and testing new topical therapies preventing and treating skin cancer in people.”

The work was funded by the National Institutes of Health (K08AR070289, P01AG031862, GM110174, CA196539, F31 GM123744-01, P30AR069589-01), the Dermatology Foundation, the Melanoma Research Foundation, and the American Skin Foundation.

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*The Perelman School of Medicine has been ranked among the top five medical schools in the United States for the past 20 years, according to U.S. News & World Report’s survey of research-oriented medical schools. The School is consistently among the nation’s top recipients of funding from the National Institutes of Health, with \$405 million awarded in the 2017 fiscal year.*

*The University of Pennsylvania Health System’s patient care facilities include: The Hospital of the University of Pennsylvania and Penn Presbyterian Medical Center — which are recognized as one of the nation’s top “Honor Roll” hospitals by U.S. News & World Report — Chester County Hospital; Lancaster General Health; Penn Medicine Princeton Health; Penn Wissahickon Hospice; and Pennsylvania Hospital – the nation’s first hospital, founded in 1751. Additional affiliated inpatient care facilities and services throughout the Philadelphia region include Good Shepherd Penn Partners, a partnership between Good Shepherd Rehabilitation Network and Penn Medicine, and Princeton House Behavioral Health, a leading provider of highly skilled and compassionate behavioral healthcare.*

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