The Epigeneticist From Wai'anae Discovers Science Behind Native Traditions |

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Epigenetics and epigenomics are big and somewhat unfamiliar words to many, but they are likely terms you will hear about more and more. Department of Native Hawaiian Health researcher and Assistant Professor Dr. Alika Maunakea's studies are helping to ensure that happens. His research in the field, detailing a link between epigenomics and alternate promoter usage, has been published in one of the world's top scientific journals, *Nature*. He also discovered another link between epigenomics and alternative pre-mRNA splicing, published recently in *Cell Research*. In playing important roles in alternate promoter usage and splicing, epigenomics contributes to the diverse pool of gene products that make us up, and, if perturbed, can lead to the development of disease.

An Epigeneticst's Work

As an epigeneticist, Dr. Maunakea studies the molecular interaction between the environment and genes, and how changes in this interaction is involved in diseases which are disproportionately prevalent in Native Hawaiian and Pacific Island populations–changes which are not due to differences in DNA sequence (i.e. genetics).

> *"DNA is a fundamental building block of genes that provide the instructions for making all of the parts of the body," Dr. Maunakea explains. "But DNA is only part of the story."*

DNA and genes make up what is called the genome, which is identical in all the body's cells. The DNA in your cells is wrapped around special proteins called histones. Both the DNA and histones are naturally covered with chemical tags collectively known as an epigenome. Different cells in the body have different epigenomes, even though the DNA remains the same.

"Although the genome is fixed for life, epigenomes are flexible and respond to signals from the environment to turn genes on or off. These "signals from the environment" can include diet and stress,

says Dr. Maunakea. Dr. Maunakea's research reveals that the epigenome not only turns genes *on or off*, it also instructs which parts of DNA in the genes are recognized and used in the cell, a normal biological process known as alternative splicing.

"We've demonstrated a new role for epigenomics in alternative splicing, and shown how both essential cellular activities are functionally linked," said Dr. Maunakea.

He said this finding has important public health implications, because abnormal alternative splicing events occur in many different diseases, including neurological disorders, diabetes, and cancer. Although the environment plays a role in these diseases, it remains unknown whether the observed abnormal alternative splicing events may arise from epigenomic alterations, as this study suggests.

"More work is needed to understand how the environment may influence the function of the epigenome on important cellular activities, such as alternative splicing, that may together contribute to disease," said Dr. Maunakea. "Further understanding may pave the way for new advances in disease diagnostics, prevention, and treatment."

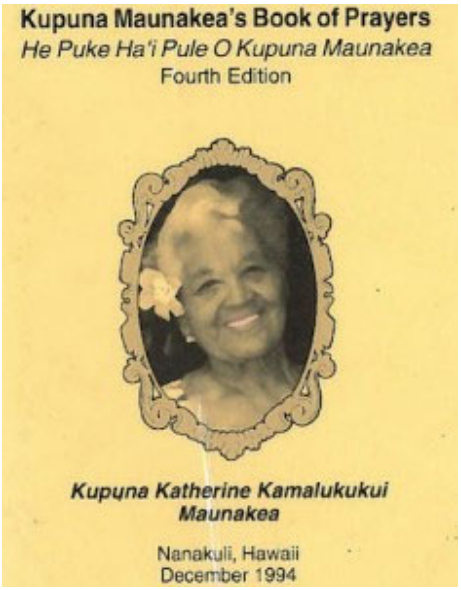
Validating Native Hawaiian Ancestral Knowledge

Born and raised in Waiʻanae, Hawaiʻi, Dr. Alika Maunakea is a Native Hawaiian biomedical researcher who has worked on epigenetic and epigenomic research in mammalian systems at the University of California San Francisco and the National Institutes of Health. He has developed and enhanced novel high-throughput technologies that survey DNA methylation and histone modifications, both central components of epigenetic processes that make up the epigenome, and has discovered novel roles for DNA methylation in regulating alternative promoter usage and in pre-mRNA splicing.

In addition to advancing the understanding of fundamental biological processes, Dr. Maunakea believes his work validates Native Hawaiian ancestral knowledge. "ʻŌlelo noʻeau (wise-sayings) abound indicate that Native Hawaiians centuries ago had an implicit understanding that the environment influences health–a fundamentally epigenetic concept. As examples, 'Pūʻali kalo i ka wai 'ole' meaning, 'Taro, for lack of water, grows misshapen' suggests that lack of caring for the land leads to illness. And 'I paʻa ke kino o ke keiki i ka lāʻau' meaning, 'that the body of the child be solidly built by the herbs', was said of mothers eating herbs (dietary supplements) during pregnancy and nursing for the sake of the baby's health in development and to help prevent adult-onset diseases."

> "*We are indeed connected to our environment, the health of which directly impacts our health as well," said Dr. Maunakea. "In an on-going community-based study where we are examining epigenomes, we are finding direct evidence in support of this ancestral knowledge," said Dr. Maunakea.*

This perspective has significant implications on the current health care system. "By integrating traditional knowledge and evidence-based methodologies, we can create new and improve on existing diagnostic methods and therapies, and enable the application of interventions designed around prevention," said Dr. Maunakea. That, he says, could shift the focus of the conventional health care model on disease treatment towards a traditional, environmentally inclusive and community-informed model of disease prevention and wellness.



Kūpuna Katherine Maunakeaʻs prayer book.

What inspires Dr. Maunakea?

“Haʻahaʻa ke kanaka no ka iʻimi naʻauao.” – Humble is the person who seeks wisdom. My great-grandmother, Katherine Maunakea, a respected kūpuna and lāʻau lapaʻau practitioner in her community in Nānākuli, taught me this ʻōlelo noʻeau when I was very young. Growing up with her influence and observing her dedicated service in the Native Hawaiian community inspired me to seek wisdom, to share it, and work collectively to apply it to the benefit of our community.”

His kūpuna continues to inspire him. That environment influences health, a focus of his research in epigenetics, is not a foreign concept to Native Hawaiians, Dr. Maunakea says. “It was my kūpunaʻs teachings of Native Hawaiian culture, values, language, medicine, and history that I have come to realize that the traditional Native Hawaiian concept of health and wellness is compatible with an epigenetic basis for development of disease. I work in biomedical sciences so that this message may inspire others from our community to see the value of our traditional knowledge, that we can continue to seek wisdom from it, and learn how to apply it to overcome the severe health challenges our community faces today for a better tomorrow.”

Dr. Maunakea’s epigenetics research ***Cell Research* (abstract)** was performed at the National Institutes of Health, Maryland; and the University of Hawaiʻi John A. Burns School of Medicine.