

Specially-bred mice help target an annual outbreak: the flu

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As part of a national collaboration, Oregon Health & Science University researchers are studying specially bred mice that are more like humans than ever before when it comes to genetic variation. Through these mice, the researchers hope to better understand and treat an infectious disease that plagues us year in and year out: the flu.

The scientists aim to determine why some people suffer serious illness and even death when infected with influenza while others suffer only mild to moderate symptoms. The research is published in a special joint issue of the journals *Genetics* and *G3: Genes, Genomes, Genetics*, both publications of the Genetics Society of America.

The research was conducted within the Pacific Northwest Regional Center for Excellence (PNWRCE) for Biodefense and Emerging Infectious Diseases, a consortium of investigators with extensive expertise, and basic and translational research capacity directed at a broad range of pathogens. The cooperative effort has the goal of combating emerging or re-emerging infectious diseases that pose a serious threat to human health. The director of the PNWRCE is Jay Nelson, Ph.D., the founder and director of the Vaccine and Gene Therapy Institute at OHSU.

For decades, [mice](#) have played a key role in developing new treatments from the discovery of penicillin to the creation of polio vaccine. Because mice studied in labs are bred in a controlled manner, they are often genetically identical. Most of the time this is beneficial. The lack of

genetic variation increases reproducibility and can help researchers more quickly determine a contributing factor to disease, but research on more complex diseases calls for mice to be more like humans who are genetically diverse. That's where this research project differs from many others.

The researchers are studying mice from the Collaborative Cross Program. Because these mice more closely reflect the [genetic variation](#) of humans, they may be the key to understanding some of today's most common, and most complex, diseases. In this case, the specially bred mice were used to study the varying immune response to the annual influenza outbreak.

In this research project, the scientists studied 44 groups of flu-infected mice that varied genetically. Due to this variation, the mouse reaction to influenza varied greatly, just as it does in the human population. The researchers then noted genetic differences that may have caused the variety of disease responses. Their ongoing work is to more clearly identify which genes cause these differences.

"Each year, annual influenza epidemics result in about 3 million to 5 million cases of severe illness," explained Shannon McWeeney, Ph.D., an associate professor of biostatistics and bioinformatics and head of the Division of Bioinformatics and Computational Biology at OHSU. "We see a broad spectrum of response to influenza infection ranging from patients with minor symptoms to the estimated 250,000 to 500,000 deaths worldwide."

"We want to understand what genetic factors influence this wide-ranging response. More importantly, with a better understanding of the genetic influence of disease response, we believe we can help in the development of better, safer vaccines that can target the most vulnerable population: the sick, elderly and young. We also want to determine if the

genetic factors that impact flu response also play a role in the varying responses to other diseases. If so, this new research method could have a much broader impact," McWeeney said.

Provided by Oregon Health & Science University

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