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Project yields major resource for scientific research

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One of the ultimate ways of understanding what impact any particular gene has in human health or disease is to disrupt it—knocking it down or wiping it out in a worm, fly or mouse and gauging what happens next.

Now scientists at the University of California, San Francisco (UCSF) Diabetes Center and the Gladstone Institute for Cardiovascular Disease have assembled a large publicly available resource to help researchers determine the importance of genes in mice and better gauge what roles they might play in disease.

Described in an upcoming issue of Cell Reports, the resource was assembled with support from the W.M. Keck Foundation and the NIH. It consists of 162 gene-disrupting vectors that target and remove pieces of DNA that encode for microRNAs—small bits of genetic material that regulate other genes. The resource also includes 64 new stem cell lines and 46 new strains of mice with missing microRNAs.

“From cancer to diabetes to immune diseases of unknown genetic nature, the project has generated a high-value resource for people out there who want to test specific ideas related to any human disease or developmental disorder,” said UCSF Associate Professor Michael McManus, PhD, who led the research.

Additional contributions came from Deepak Srivastava, director of the Gladstone Institute for Cardiovascular Disease, and Pieter DeJong at the Children’s Hospital Oakland Research Institute. UCSF immunologists

Jeff Bluestone, Abul Abbas, Lewis Lanier and Art Weiss are co-investigators for this project. McManus is director of the W.M. Keck Center for Noncoding RNAs at UCSF.

How the Resource Was Created

MicroRNAs reside in a part of the genome known as "junk DNA"—because the scientific community once thought vast swaths of DNA in the human genome contained no genes. But since the human genome was decoded at the turn of this century, that view has crumbled.

Even though this "junk DNA" does not code for genes, it makes a rich number of microRNAs. All organisms on earth, from fruit flies to Fillmore Street musicians, have a large number of these microRNAs in their junk DNA.

Scientists around the world are now studying the roles these microRNA may play in the biology of human diseases, McManus said. Much of this work involves tinkering with microRNAs in cells grown in the laboratory, he added, but the ultimate way to study them is to knock them out in an organism like the mouse or the fruit fly. That's why he and his colleagues created the new resource.

Additional support was provided through a Swiss National Science Foundation fellowship, a JDRF Scholar Award, and an American Cancer Society Professorship.

More information: The article, "A Resource for the Conditional Ablation of microRNAs in the Mouse" by Chong Yon Park, Lukas T. Jeker, Karen Carver-Moore, Alyssia Oh, Huey Jiin Liu, Rachel Cameron, Hunter Richards, Zhongmei Li, David Adler, Yuko Yoshinaga, Maria Martinez, Michael Nefadov, Abul K. Abbas, Art Weiss, Lewis L. Lanier, Pieter J. de Jong, Jeffrey A. Bluestone, Deepak

Srivastava, and Michael T. McManus appears in the April 26 issue of *Cell Reports*.

Provided by University of California, San Francisco