New study solves mouse genome dilemma

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Laboratory research has always been limited in terms of what conclusions scientists can safely extrapolate from animal experiments to the human population as a whole. Many promising findings in mice have not held up under further experimentation, in part because laboratory animals, bred from a limited genetic foundation, don't provide a good representation of how genetic diversity manifests in the broader human population.

Now, thanks to an in-depth analysis by a team led by Fernando Pardo-Manuel de Villena, PhD, in the UNC Department of Genetics and Gary Churchill, PhD, at The Jackson Laboratory in Bar Harbor, Maine, researchers will be able to use an online resource dubbed the Mouse Phylogeny Viewer to select from among 162 strains of laboratory mice for which the entire genome has been characterized. Phylogeny refers to the connections among all groups of organisms as understood by ancestor/descendant relationships. Pardo-Manuel de Villena is also a member of UNC Lineberger Comprehensive Cancer Center and the Carolina Center for Genome Sciences.

The results of the analysis that make this tool possible were published online today in the journal Nature Genetics.

"The viewer provides scientists with a visual tool where they can actually go and look at the genome of the mouse strains they are using or considering, compare the differences and similarities between strains and select the ones most likely to provide the basis for experimental results that can be more effectively extrapolated to the diverse human

population," said Pardo-Manuel de Villena.

"As scientists use this resource to find ways to prevent and treat the genetic changes that cause cancer, heart disease, and a host of other ailments, the diversity of our lab experiments should be much easier to translate to humans," he noted.

He explains that the DNA of a given pair of typical laboratory mouse strains varies in only half of their genome and captures less than 20 percent of the diversity of the entire mouse genome. Historically, biomedical researchers have relied on what are called classical inbred strains of mice in laboratory research. With the advance of genetic science, researchers began to use wild-derived laboratory strains (descendants of captured wild mice that originate from a small number of original ancestors) to try to overcome issues associated with limited genetic diversity. However, scientists' understanding of genetic diversity in mice has – until now – been limited and biased toward the most frequently used strains.

The team compared the genome of a large and diverse sample including 36 strains of wild-caught mice, 62 wild-derived laboratory strains and 100 classical strains obtained from different stocks and different laboratories using the Mouse Diversity array – a technology that maps the entire mouse genome.

Their analysis exponentially increases the data available to geneticists who work with mice, allowing them to statistically impute the whole mouse genome sequence with very high accuracy for hundreds of laboratory mouse strains – leading to much greater precision in the interpretation of existing biomedical data and optimal selection of strains in future experiments.

More information: Subspecific origin and haplotype diversity in the

laboratory mouse. *Nature Genetics*, advance online publication Sunday, May 29, 2011, dx.doi.org/10.1038/847