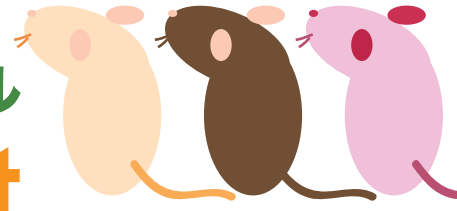
The 133rd RIKEN BRC SEMINAR

Since 1917 BRC

2016年2月9日(火) 13:30～14:30

バイオリソースセンター1階　森脇和郎ホール



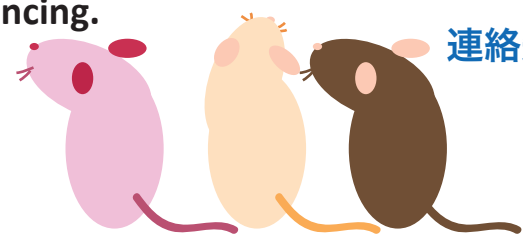
Dr.Laura Reinholdt

Senior Research Scientist, The Jackson Laboratory

Dr. Laura G. Reinholdt is co-director of Genetic Resource Science, which is home to the JAX Repository, a collection of over 8,000 unique mouse strains. Her research interests are in the development and application of genetic and genomic approaches for understanding the etiology of genome variation and the role of genome variation in health and disease. As the lead scientist on several large mouse model development programs, including the Mouse Mutant Regional Resource Center, she has expertise in the development and credentialing of mouse models of human disease. She is recognized for her pioneering efforts to use high throughput sequencing to identify causative mutations in over 200 mouse models of Mendelian disease.

Forward genetic approaches for Mendelian disease modeling in mice

Spontaneously arising mouse mutations have served as the foundation for understanding gene function for more than 100 years. We have utilized exome sequencing to identify the causative mutations in nearly 200 mouse models of Mendelian disorders, including a broad range of clinically relevant phenotypes. To analyze the resulting data, we developed an analytics pipeline that is optimized for mouse exome data and a variation database that allows for reproducible, user-defined data mining as well as nomination of mutation candidates through knowledge-based integration of sample and variant data. Using these tools, we identified putative pathogenic mutations for over half of the strains in our study. Despite the increased power offered by potentially unlimited pedigrees and controlled breeding, about half of our exome cases remained unsolved. Using a combination of manual analyses of exome alignments and whole-genome sequencing, we found evidence that a large fraction of unsolved exome cases have underlying structural mutations. This result directly informs efforts to investigate the similar proportion of apparently Mendelian human phenotypes that are recalcitrant to exome sequencing.



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