Keynote Lecture XII

Comparative Genomic and CHIP-SEQ Success in Predicting In Vivo Activity of Human Enhancers

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Internationally recognized geneticist, Dr Eddy Rubin has served since 2002 as Director of the U.S. Department of Energy Joint Genome Institute (JGI), and Director of the Genomics Division at Lawrence Berkeley National Laboratory (LBNL). With more than 200 peer-reviewed publications -- over 30 in the leading journals Science and Nature, his research focuses on the development of computational and biological approaches for studying genomes.

Under Dr Rubin's leadership, the JGI, one of the world's five leading institutions responsible for sequencing the human genome, completed and published the DNA sequence of human chromosomes 5, 16, 19. He has played a major role both nationally and internationally advancing genome sciences including serving as co-chair of the Cold Spring Harbor Symposia on the Genome of Homo Sapiens and as a scientific chair of the International Human Genome Organization. Completing DOE's commitment to the Human Genome Project in 2004, Dr Rubin directed the JGI's focus to the sequencing and analysis of organisms of relevance to bioenergy, carbon cycling, and bioremediation. This scientific focus of the JGI is described in his recent review, "Genomics of cellulosic biofuels", published in the journal *Nature*.

Dr Rubin received his BA degree in physics from the University of California, San Diego, his PhD in biophysics from the University of Rochester, and his MD also from the University of Rochester. Following a genetics fellowship at the University of California, San Francisco, he became a research associate at the Howard Hughes Medical Institute. Dr Rubin Joined LBNL in 1988 and led the Laboratory's Genome Sciences Department from 1998 to 2002.

Dr Rubin has directed several large federally-funded research programs, among them the Program for Genomic Applications supported by the National Institutes of Health (NIH), a major initiative to advance functional genomic research related to heart, lung, and blood disorders. Dr Rubin's studies emphasized the use of large-scale cross-species DNA sequence comparisons to identify regions of the human genome that encode important biological functions. His groundbreaking work on evolutionarily conserved noncoding regions helped highlight the utility

of genome comparisons to decode gene regulation. The Rubin Laboratory has also pioneered the genetic engineering of mice subsequently used as animal models for common human disorders including sickle cell anemia, atherosclerosis, and asthma.

More recently, Dr Rubin and his JGI collaborators have played a leading role in the emerging field of metagenomics -- sequencing and characterizing DNA extracted directly from environmental samples -- to obtain an overview of community function and population dynamics. The environments studied included termite hind guts, gutless worms, acid mine drainage sites and 40,000 year old Neanderthal remains.

Dr Rubin is on editorial boards of several leading journals including serving as a member of the Board of Reviewing Editors for the journal *Science*.

He participates in an advisory role for many large-scale scientific enterprises in the US and abroad, including The Wellcome Trust Sanger Institute, Genome Canada, Chancellor's Advisory Board of University of California at Davis, and the Genome Institute of Singapore.

Dr Rubin has been active in training the next generation of scientists. This is in part evident in his mentorship of over 50 post-doctoral fellows, many of whom are now faculty members of leading academic and research institutions in the US and abroad.

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Transcriptional enhancers are key gene regulatory elements that can act over large distances and play important roles in human development and disease. While evolutionary conservation of non-coding sequences between species has provided a signal for their detection, predicting the spatial and temporal activity patterns of enhancers in vivo remains a major challenge. To address this issue, we have explored the use of chromatin immunoprecipitation directly from several embryonic mouse tissues, coupled with sequencing to selectively identify in vivo enhancers active in a given tissue. From the computational analyses of several gigabases of ChIP DNA, we identified thousands of genomic regions enriched in transcriptional co-activator binding and tested a large number in transgenic mouse assays. Our results indicate that ChIP-seq directly from tissues is an effective means for identifying and predicting the spatial and temporal activity of vertebrate enhancers.