B·DEBATE International Center for Scientific Debate BARCELONA

CRG Centre for Genomic Regulation

BIOLA-MARIA JAVIERRE

ABSTRACT

PARTICIPANT AT:

CODING AND NON-CODING FUNCTIONS OF THE GENOME
BARCELONA CONFERENCE ON EPIGENETICS AND CANCER

October, 29th-30th, 2015, Barcelona

Biola-Maria Javierre, The Babraham Institute, Cambridge, UK

Short talk: "Genomic Regulatory Architecture in Human Haematopoiesis Links Disease-Associated Variants with Their Target Genes"

Three-dimensional chromatin organization plays a major role in metazoan gene regulation, but understanding of the dynamic nature of genome architecture across cell types and its effect on cellular commitment is incomplete. Here, we use Promoter-Capture Hi-C to identify distal sequences interacting with 22,225 known promoters in 17 primary human haematopoietic cell types. With a total coverage of more than 11 billion unique, promoter contacts we detect 2,816,292 significant long-range, promoter interactions involving 247,962 potential regulatory elements that drive blood cell gene regulatory programs. Clustering patterns of promoter interactions reconstructs the hematopoietic lineage tree demonstrating robust and dynamic cell-type specific chromatin architecture. More than half of the interactions are cell-type or lineage-specific, and preferentially link actively transcribed promoters with active distal enhancers. The remaining, generally tissue-invariant interactions are depleted of gene regulatory features, potentially playing non-canonical roles in gene regulation. We further show that promoter-interacting regions are strongly and tissue-specifically enriched for non-coding GWAS SNPs associated with common diseases. Using a Bayesian approach to prioritise target genes underlying GWAS traits we identify dozens of trait-associated genes that include both known and novel candidates, providing a potential breakthrough in understanding of the mechanisms underlying multiple genetic diseases and traits.

B·DEBATE IS AN INITIATIVE OF:

biocat "la Caixa" Foundation