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Δαρβινική Δευτέρα με θέμα

From genomics to therapeutics: Single-cell dissection and manipulation of disease circuitry

Disease-associated variants lie primarily in non-coding regions, increasing the urgency of understanding how gene-regulatory circuitry impacts human disease. To address this challenge, we generate comparative genomics, epigenomic, and transcriptional maps, spanning 823 human tissues, 1500 individuals, and 20 million single cells. We link variants to target genes, upstream regulators, cell types of action, and perturbed pathways, and predict causal genes and regions to provide unbiased views of disease mechanisms, sometimes re-shaping our understanding. We find that Alzheimer's variants act primarily through immune processes, rather than neuronal processes, and the strongest genetic association with obesity acts via energy storage/dissipation rather than appetite/exercise decisions. We combine single-cell profiles, tissue-level variation, and genetic variation across healthy and diseased individuals to map genetic effects into epigenomic, transcriptional, and function changes at single-cell resolution, to recognize cell-type-specific disease-associated somatic mutations indicative of mosaicism, and to recognize multi-tissue single-cell effects of exercise and obesity. We expand these methods to electronic health records to recognize multi-phenotype effects of genetics, environment, and disease, combining clinical notes, lab tests, and diverse data modalities despite missing data. We integrate large cohorts to factorize phenotype-genotype correlations to reveal distinct biological contributors of complex diseases and traits, to partition disease complexity, and to stratify patients for pathway-matched treatments. Lastly, we develop massively-parallel, programmable and modular technologies for manipulating these pathways by high-throughput reporter assays, genome editing, and gene targeting in human cells and mice, to propose new therapeutic hypotheses in Alzheimer's, obesity, and cancer. These results provide a roadmap for translating genetic findings into mechanistic insights and ultimately new therapeutic avenues for complex disease and cancer.

Δευτέρα 4 Οκτωβρίου 2021, 7 μμ.

Οι διαλέξεις θα γίνονται online μέσω της πλατφόρμας ZOOM (<https://zoom.us/j/97078540320>) με δυνατότητα παρέμβασης και ερωτήσεων από το «ακροατήριο». Πληροφορίες αναφέρονται στην ιστοσελίδα <https://darwinianmondaysgr.weebly.com>. Όσοι επιθυμούν πρόσθετη τεχνική βοήθεια μπορούν να απευθυνθούν στο dm.help2020@gmail.com. Προσβλέπουμε σε μια «ζωντανή» και γόνιμη τηλε-συμμετοχή.