A Map of the Connectivity Map

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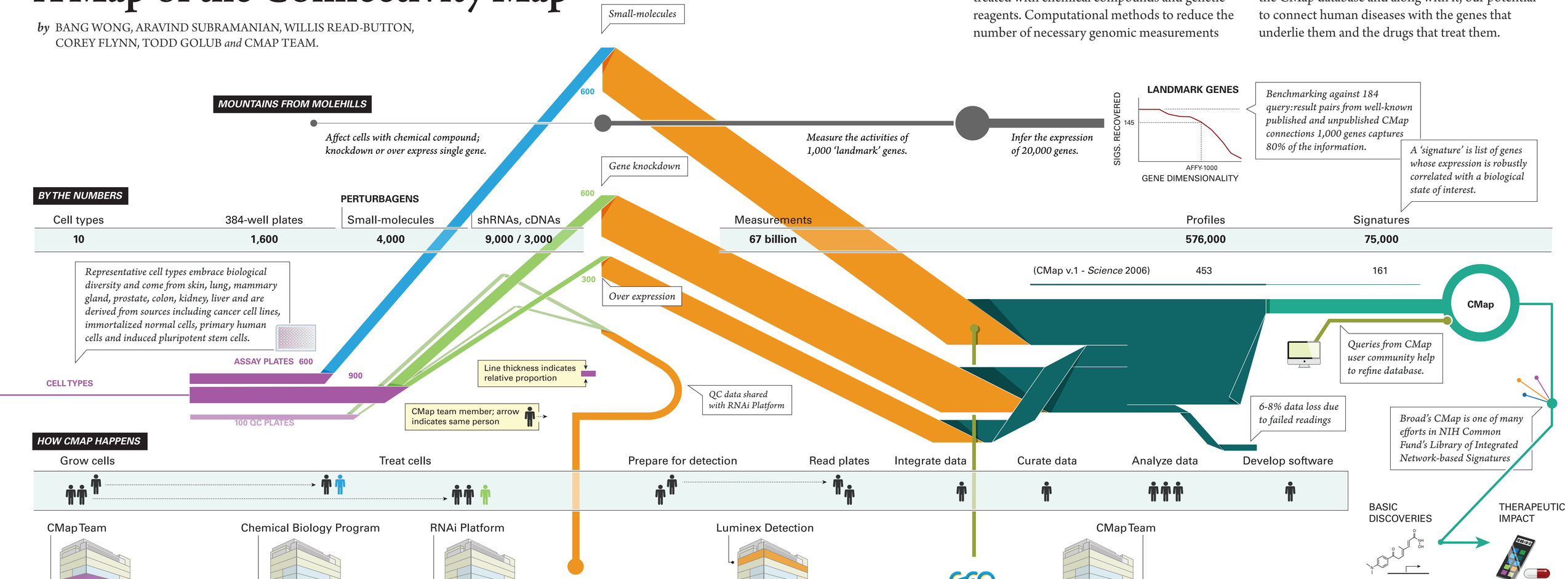
Abstract: The *Connectivity Map* is a catalog of gene-expression data collected from human cells treated with chemical compounds and genetic reagents. Computational methods to reduce the number of necessary genomic measurements along with streamlined methodologies enable the current effort to significantly increase the size of the CMap database and along with it, our potential to connect human diseases with the genes that underlie them and the drugs that treat them.



TISSUE CULTURE

A panel of normal, cancer and primary cells provides diverse biological contexts to investigate the transcriptional effects of cellular perturbation. Ten (10) additional cell lines will be profiled in 2012.

CHEMICAL PERTUBATION

Compound Management at Broad provides a consolidated, QC'd source for chemical matter, and prepares custom plated chemical libraries for the CMap. Coumpounds are selected from NIH's Clinical Collection, MLPCN and novel chemistry from Chemical Biology's DOS library.

GENETIC PERTUBATION

The RNAi platform generates lentiviral shRNA constructs that knock down target transcript expression and lentiviral cDNAs of open reading frames that cause gain-of function of selected genes. Genes chosen for genetic perturbation are derived from known targets of drugs, well-studied pathways and canonical disease genes nominated by the community including GWAS, TCGA and 1000 genomes project.

QUANTIFY RNA LEVELS

The L1000 assay enables rapid quantification of gene expression levels for 1,000 transcripts per sample in 384-well format. It is a cost-effective and scalable platform to generate large amounts of transcriptional data.

DATA PIPELINES

The CMap data pipeline streamlines data normalization, annotation and generation of the inferred gene expression values to provide whole-genome expression data for each sample.

BUILDING CONNECTIONS

CMap intends to accelerate the discovery process by systematically revealing connections between genes/compounds discovered in screens and molecular pathways that underly disease states. The goal is to turn basic discoveries into drugs and diagnostics that have therapeutic impact.

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