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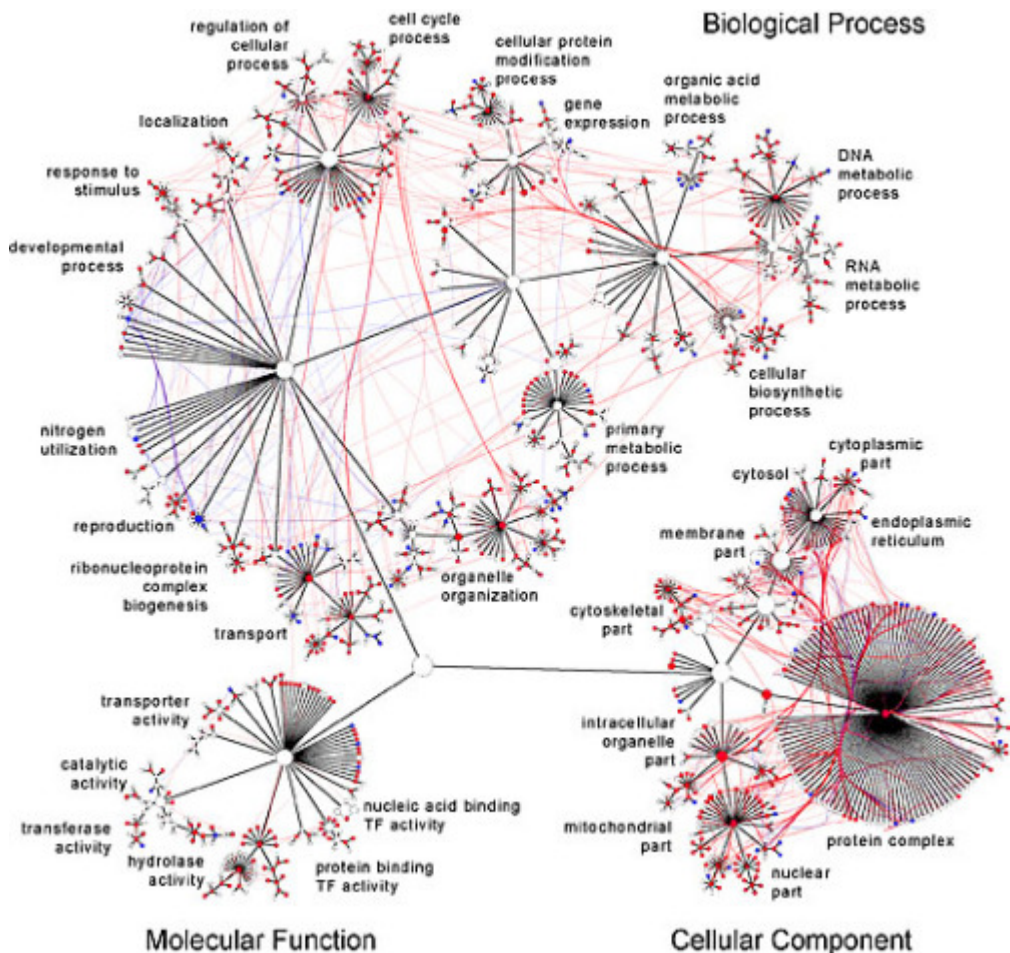
#ontology

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## JUST THE FAQs: Connecting Genotype to Phenotype with “Ontotype”

Biologists have long tried to unravel how an individual’s genetic makeup (genotype) will give rise to physical traits such as height, eye color or risk for a disease (phenotype). It can be tricky using genotype to predict phenotype — in complex organisms, a particular phenotype can’t always be traced back to a single gene or even a single part of a chromosome. Likewise, different variations in DNA sequence, even dispersed across the genome, can result in similar phenotypes.

To translate genotype to phenotype, researchers need to account for the functional impact of genetic variation on many different levels within a cell. To help do this, [Trey Ideker, PhD](#), Michael Ku Yu, a graduate student in Ideker’s University of California, San Diego School of Medicine lab, and their team

devised a new computational model that interprets what they've dubbed a cell's "ontotype." This approach is published February 24, 2016 by the journal *Cell Systems*. JUST THE FAQs explains ...

### **What's an ontotype?**

In many fields, ontology is a way to factor prior knowledge into a hierarchy of increasingly specific concepts. That's how Apple's Siri and IBM's Watson carry out logical reasoning, for example.

The Ideker and Yu team's ontotype refers to existing knowledge of how cells work — from miniscule variations in DNA sequence to functional changes in proteins, protein complexes, cellular process, organelles, and, ultimately, phenotypic behaviors of cells, tissues and complex organisms. Ontotype cuts across all of these scales to create a hierarchy of disruptions that represent the effects of genetic variations on a cell at many phenotypic levels.

### **What does an ontotype look like in the lab?**

Ideker, Yu and team developed a computational model that applies logic rules to use ontotype to predict phenotype. They used their new system — a sort of "ontotype translator" — to simulate how fast the yeast *Saccharomyces cerevisiae* (the type often used in baking and brewing) will grow when particular genes in its genome are mutated. The system accurately predicted the growth outcomes of 2,503 double gene deletions in yeast that impacted DNA repair or other basic cellular functions.

Although past models have applied similar intuition, the team took this idea a step further by examining how subsystems are themselves cooperating within larger systems, and so forth in a deep hierarchy within the cell.

"The secret sauce to our model is to examine not only how a gene functions alone, but also how it cooperates with other genes in components, processes and other subsystems within a cell," Yu said.

### **What do ontotypes mean for complex genetic diseases?**

Moving forward beyond yeast, Ideker and Yu believe that the modeling principles demonstrated in this study could also be applied to advance our understanding of human genetics and diseases.

"Our goal is to develop a new type of medicine based on knowledge of the complete physical and functional wiring of the cell," said Ideker, who is professor of medicine and bioengineering, and chief of the Division of Medical Genetics at UC San Diego School of Medicine.

*Pictured: Visualization of cellular structure and function helps researchers make predictions. Image courtesy of Cell Systems.*

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