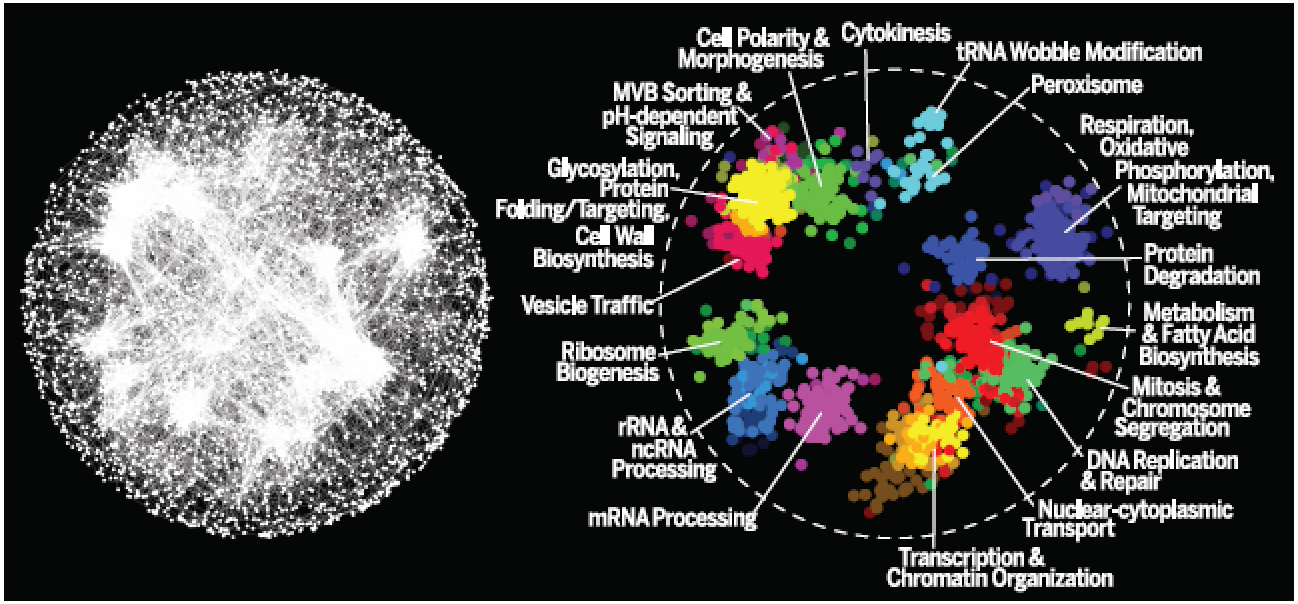
A global genetic interaction network maps a wiring diagram of cellular function



报告人：江帆

Background

- a new map of cell-gene interactions from yeast cells for 15 years .
- the first time how genes interact in group and to explains how hundreds of thousands of genes coordinate with each other and carefully arrange cell life.
- It provides a reference guide for mapping gene interaction in human cells.

Note

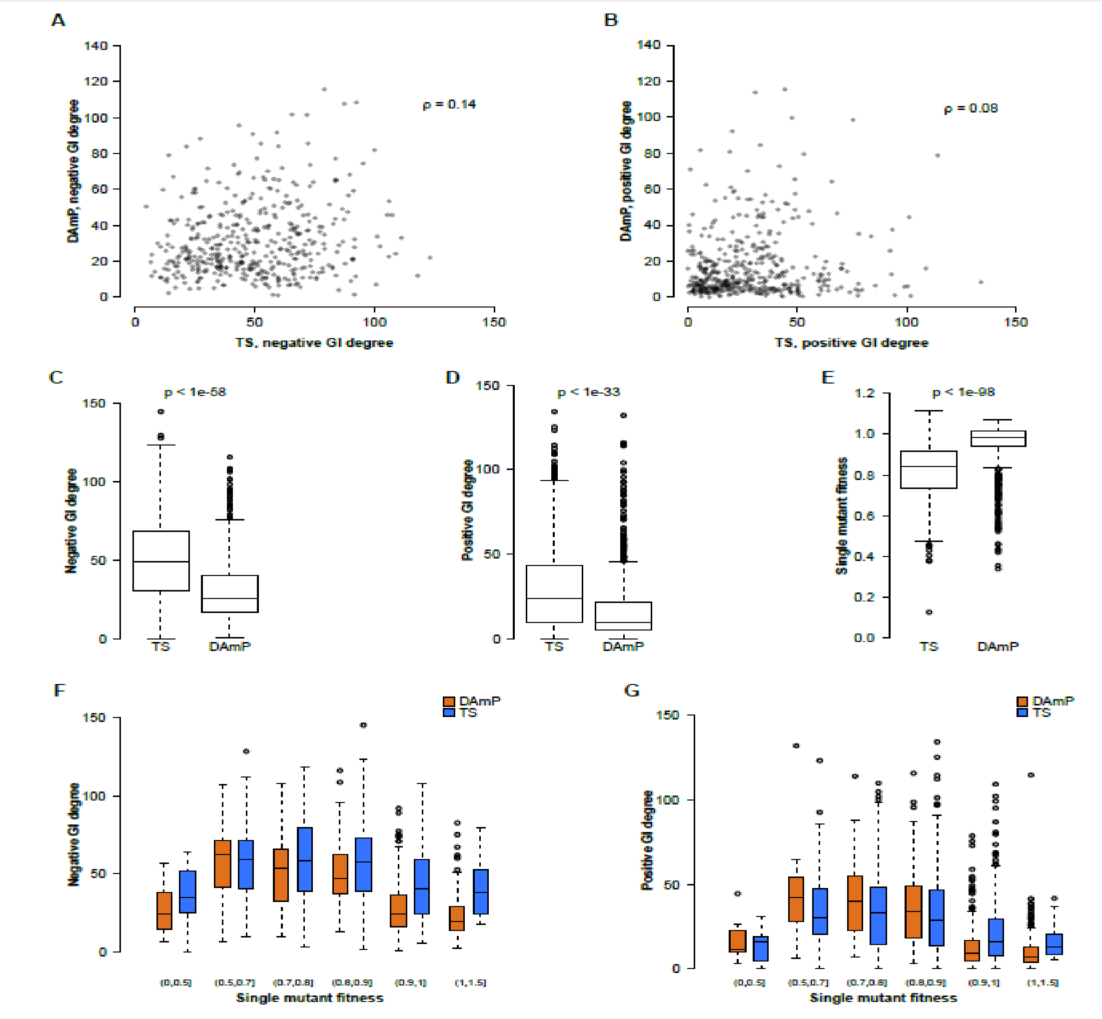
- gene pairs
- essential genes
- nonessential genes
- negative genetic interactions
- positive genetic interactions

Materials and Methods

- **Materials：** Saccharomyces cerevisiae
- **Methods：** Synthetic genetic array (SGA)
- 1. generated a genome-scale library of natMX-marked deletion mutant query strains and crossed them to an array composed of the corresponding kanMX-marked deletion mutant collection.(nonessential genes)

- 2. TS mutants were screened at a semipermissive temperature and constructed a set of essential gene query strains carrying decreased abundance of mRNA (DAmP) alleles.(essential genes)

Comparison of genetic interaction trends for DAmP and TS alleles



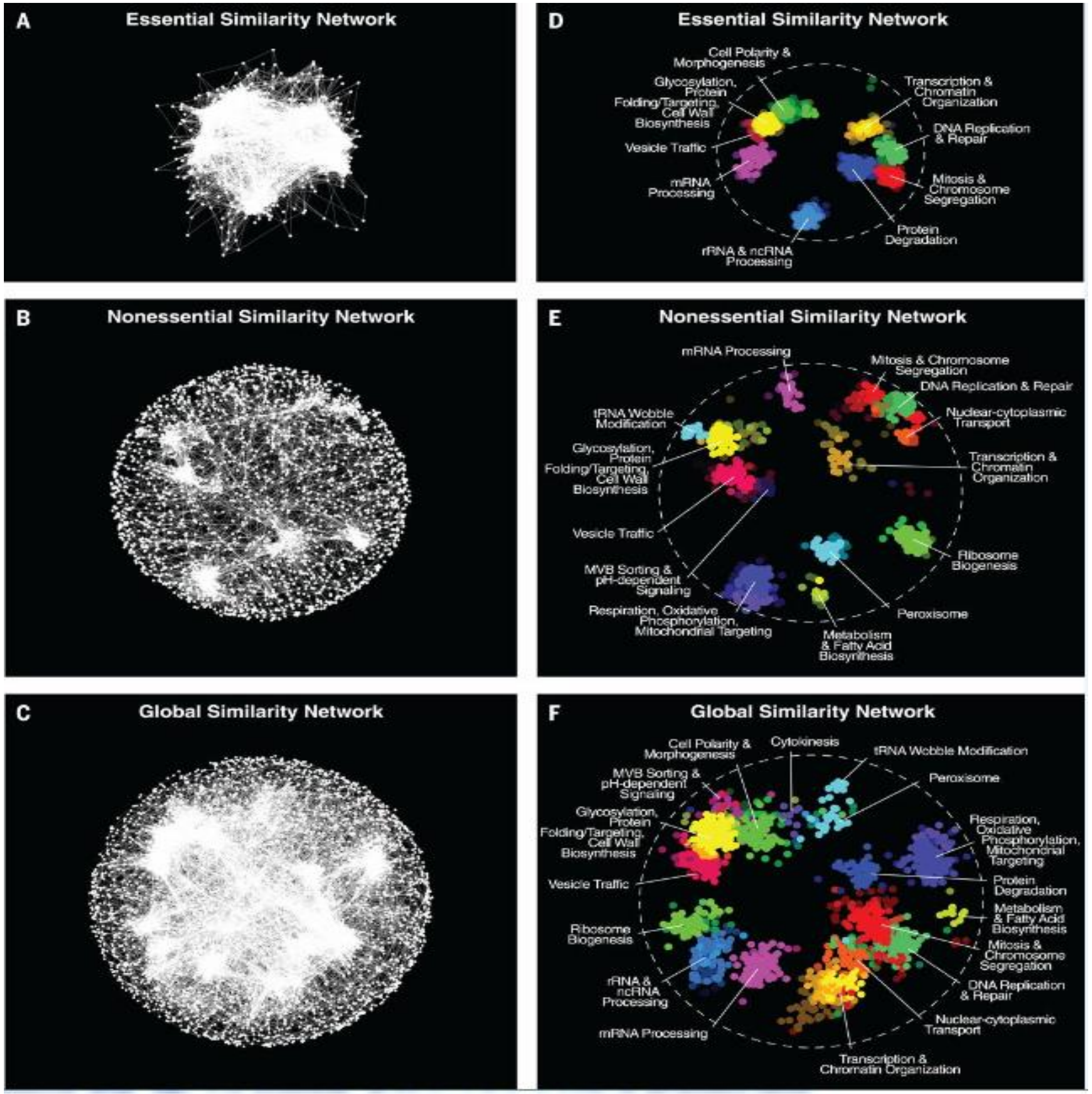
DAmP alleles exhibited fewer interactions compared with TS alleles of essential genes

TS alleles mediated the majority of the essential gene genetic interactions in our network

1.A functional map of a cell

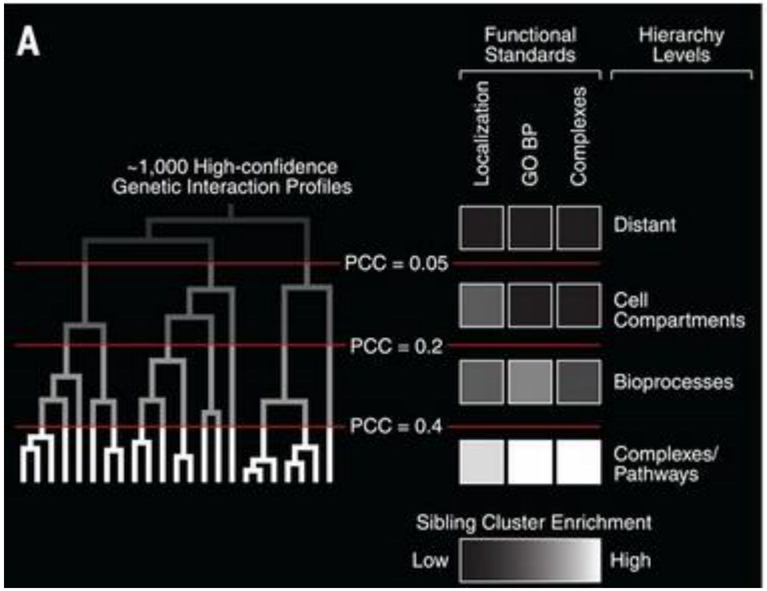
- NxN: nonessential deletion mutant query strains was screened against the nonessential deletion mutant array.
- ExN: query strains carrying TS alleles of essential genes were also screened against the nonessential deletion mutant array.
- ExE: both nonessential deletion mutant and TS query mutant strains were crossed to an array of TS strains of essential genes.

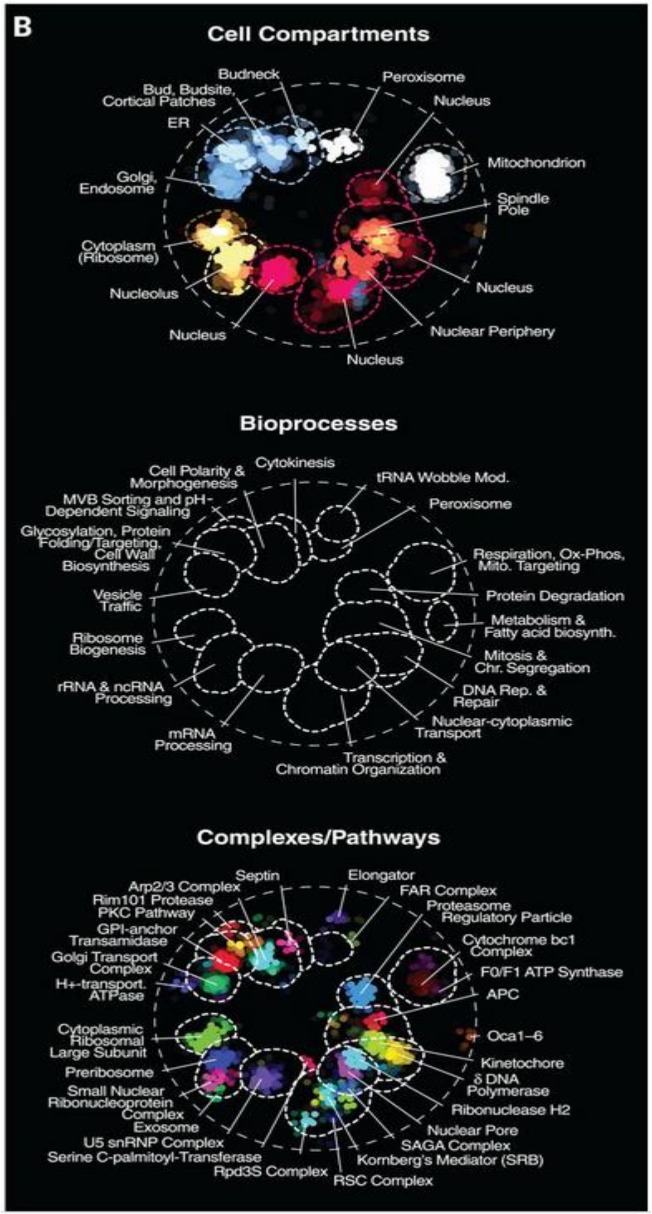
A global network of genetic interaction profile similarities



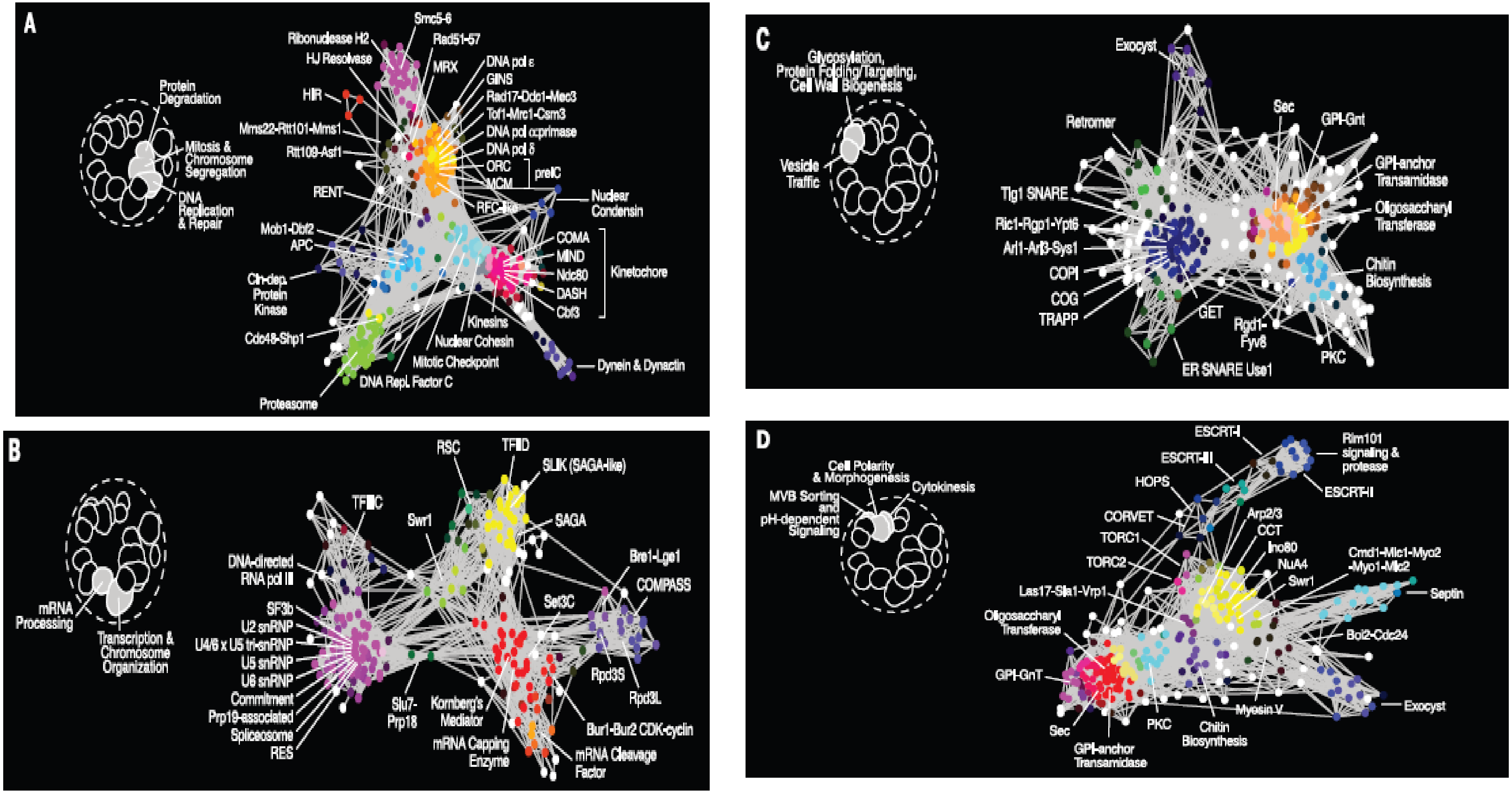
SAFE: spatial analysis of functional enrichment

2. Genetic profile similarities map a hierarchy of gene and cellular function

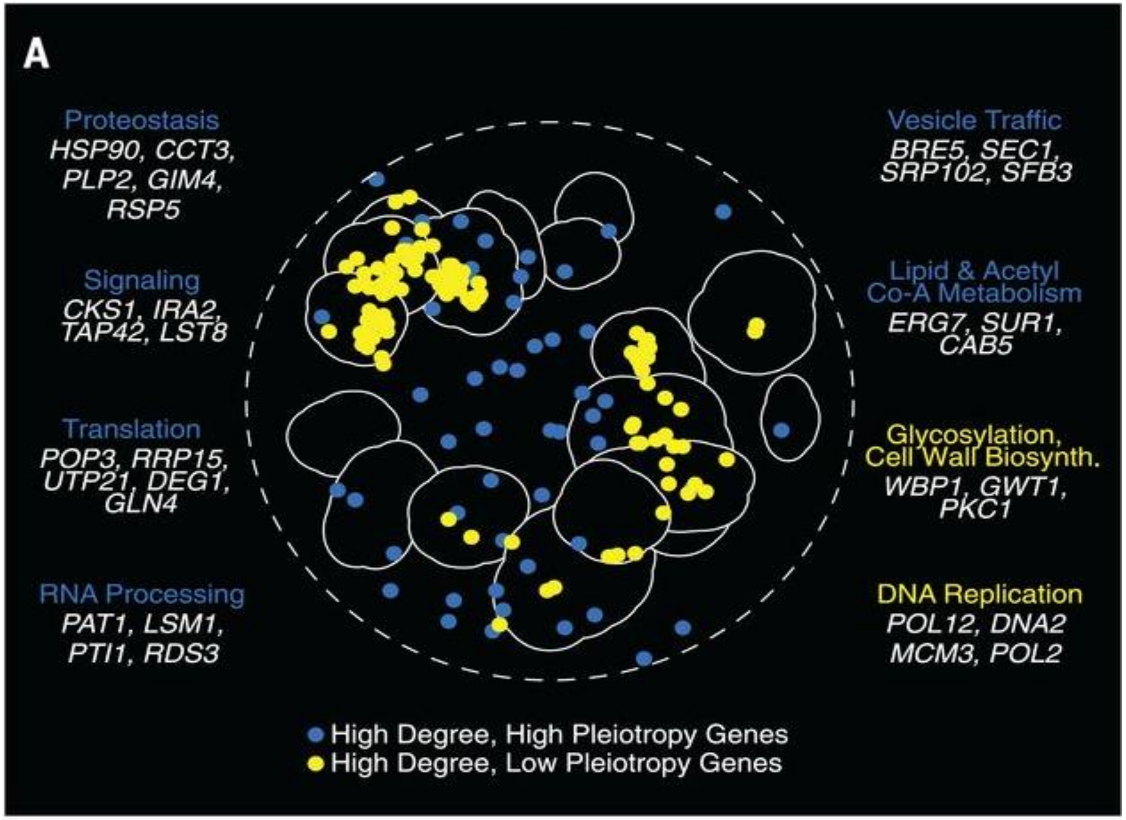




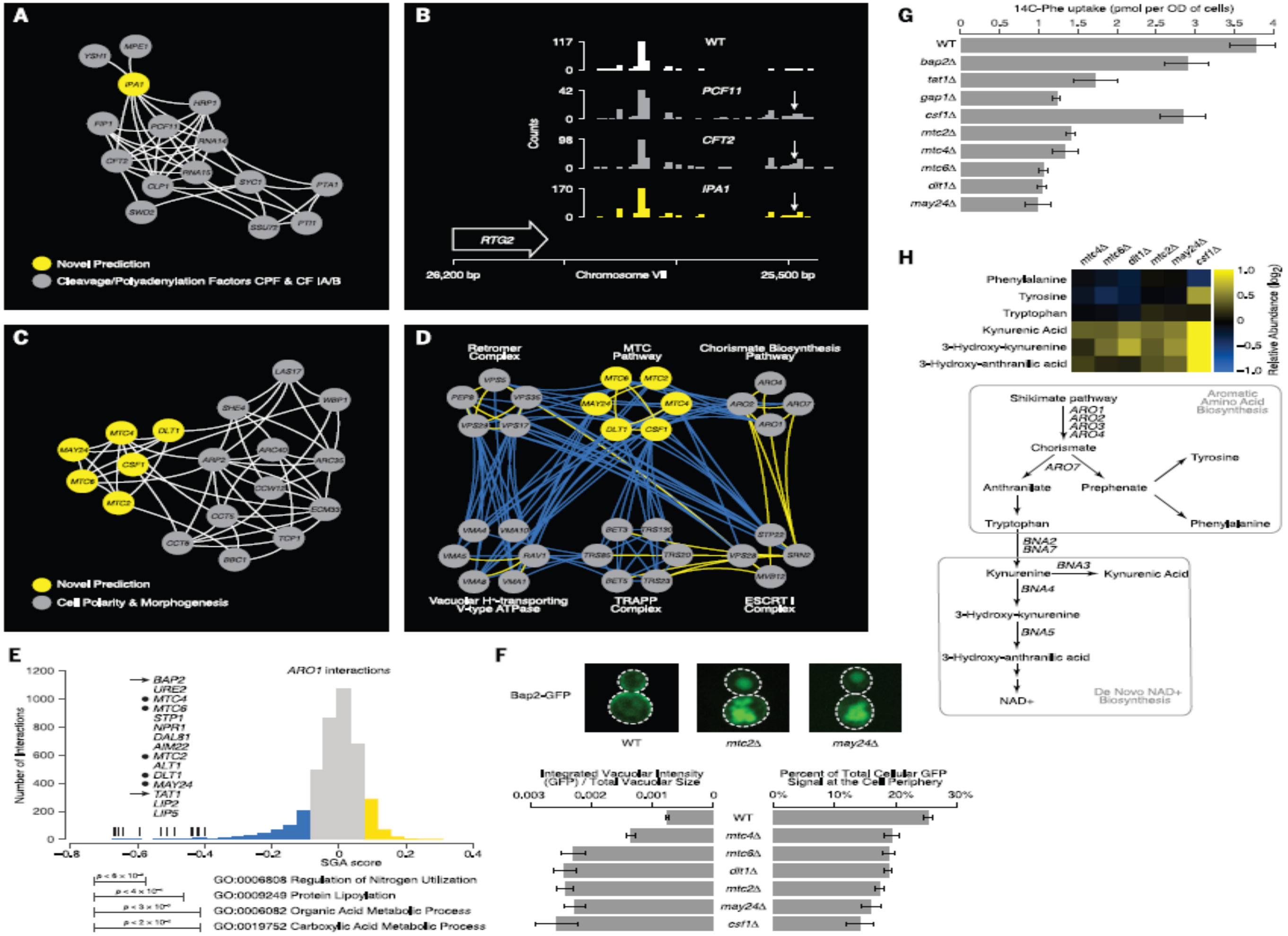
Genetic interaction profile similarity subnetworks



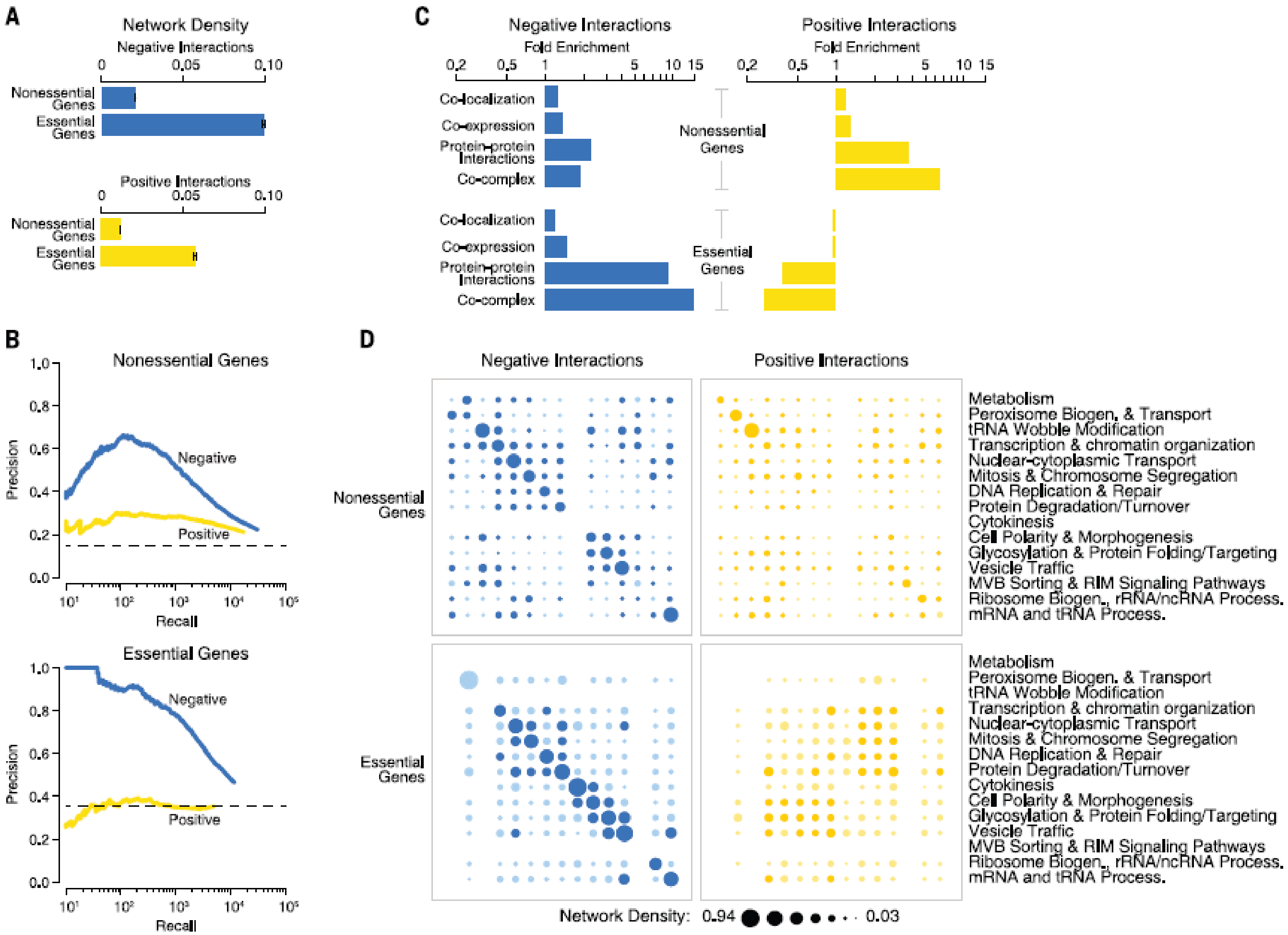
3. **Quantifying genetic pleiotropy**



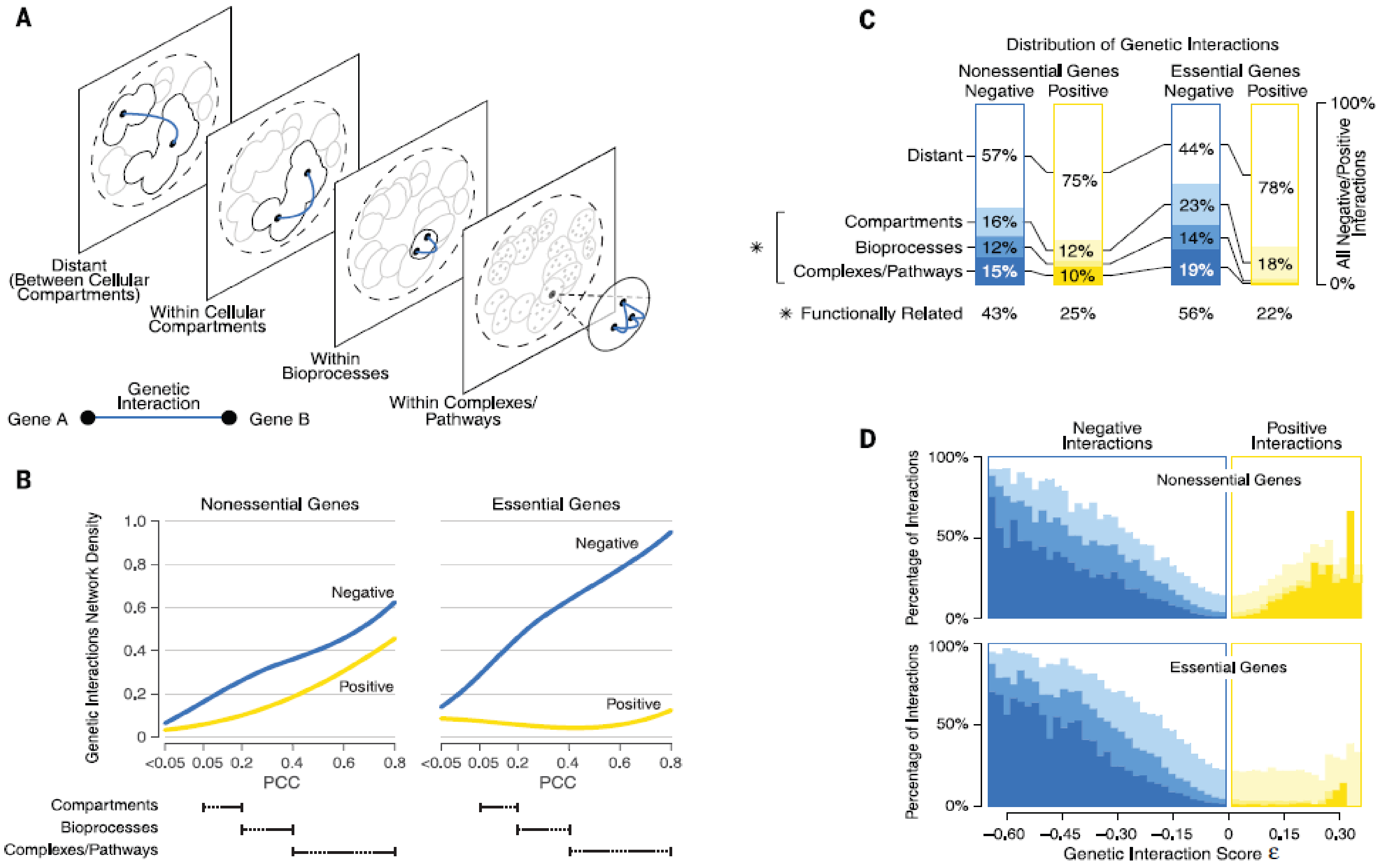
4. Predicting novel gene function



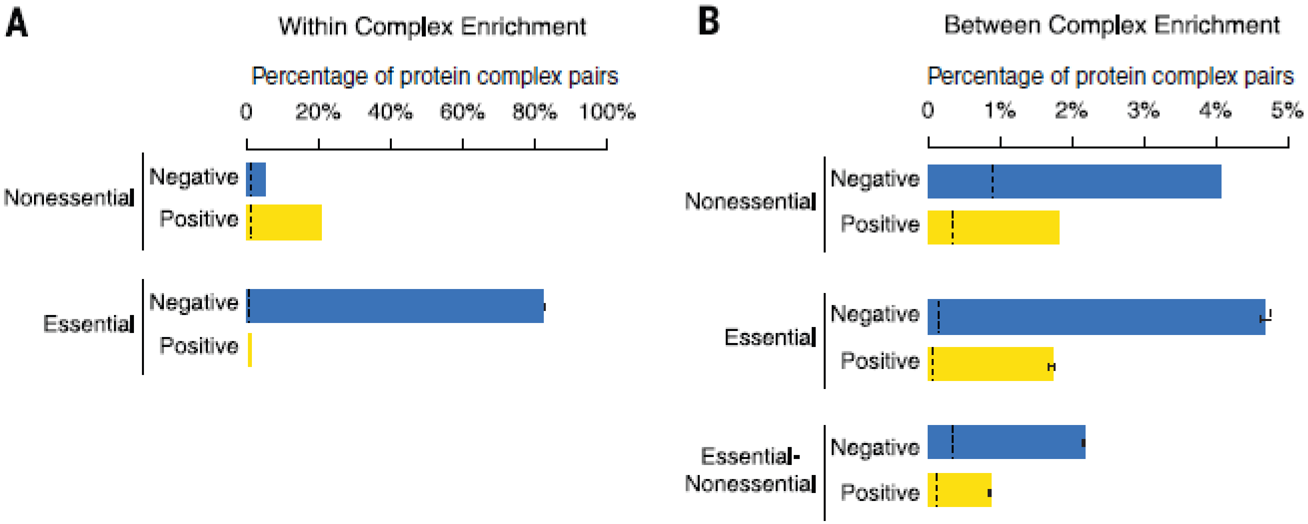
5. Negative and positive genetic interactions of essential and nonessential genes



6. The architecture of negative/positive interactions within the genetic network hierarchy

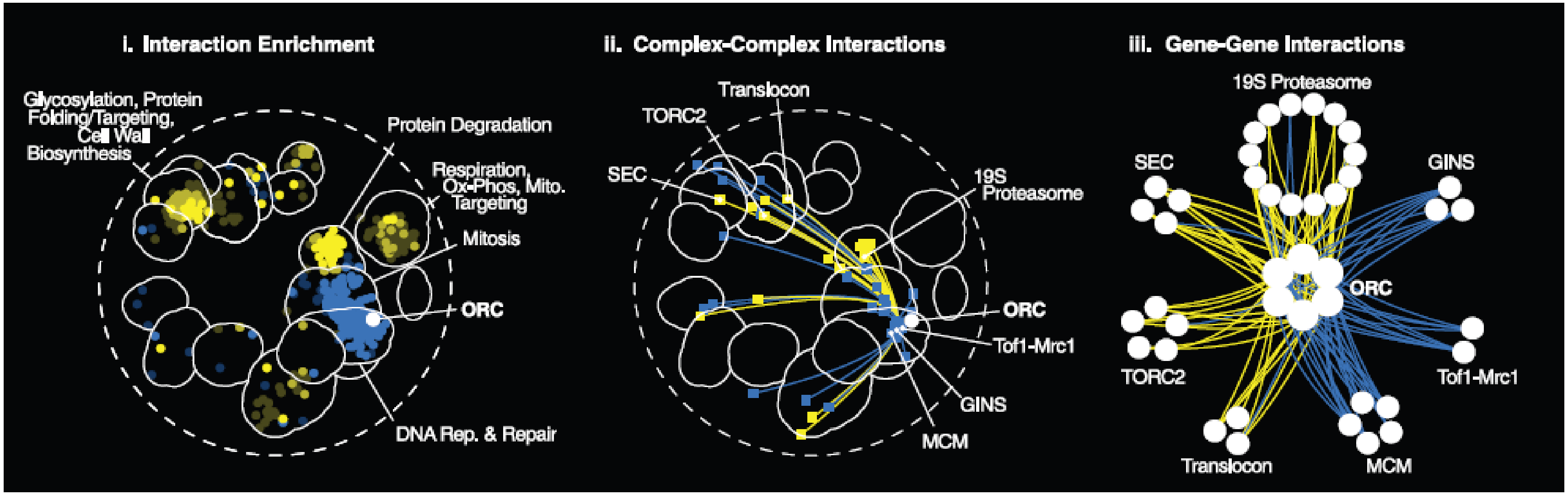


7. Genetic interactions within and between protein complexes

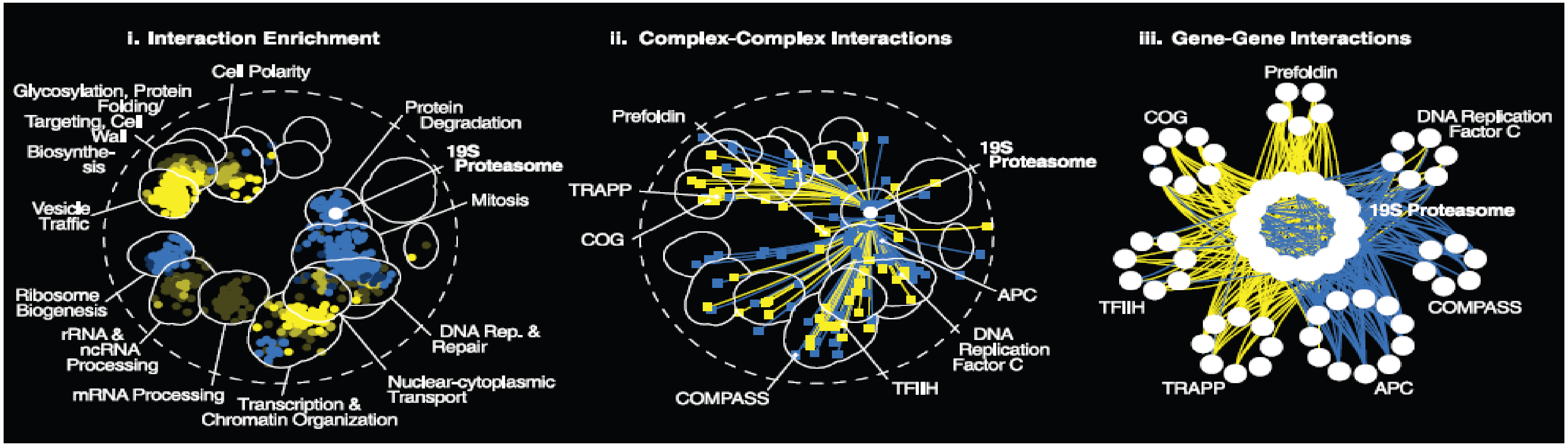


8. Functional wiring diagrams of protein complexes

A Origin Recognition Complex (ORC)



B 19S Proteasome Regulatory Particle



Conclutions

- 1. identifying nearly 1 million interactions, including ~550,000 negative and ~350,000 positive interactions.
- 2. essential genes were network hubs, displaying five times as many interactions as nonessential genes.
- 3. a global network based on genetic interaction profile similarity revealed a hierarchy of modules reflecting the functional architecture of a cell.
- 4. negative interactions connected functionally related genes, mapped core bioprocesses, and identified pleiotropic genes, whereas positive interactions often mapped general regulatory connections associated with defects in cell cycle progression or cellular proteostasis.
- 5. the global network illustrates how coherent sets of negative or positive genetic interactions connect protein complex and pathways to map a functional wiring diagram of the cell.

- 创新点：与之前报道过的图谱不同，这张关于酵母新图谱首次展示了基因如何以小组的形式相互作用，并首次以基因对为单位，解释了成千上万的基因如何互相协调，精心安排细胞的生活 ，这一成果为探索基因如何导致疾病开辟了新的途径，有望帮助开发精准的治疗方法。

- 不足：虽然这篇文献首次以基因对为单位，成对删除酵母细胞中的2个基因并试图找到对生存至关重要的基因对，然而开展这样的工作需要对酵母中6000多个基因中不同组合进行刷选，这么大量的工作文章并没有过多的去提及。

- 启发：通过了解酵母这个简单细胞模型的基因网络互作图谱是如何绘制的，我们可以为开始绘制人类细胞的基因互作图谱，甚至可以扩大到不同的细胞类型中的图谱提供了一份参考指南。

Thanks