

Focusing in on high-resolution network biology

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A central challenge in genetics is to understand how changes in DNA result in observable changes in an organism; how genotype maps to phenotype. As genes and their protein products do not act in isolation, connecting genotype with phenotype requires thinking of genes in their network context.

Traditionally, network biology has treated [genes](#) and proteins as simple nodes in a network, ignoring their structural properties. This type of 'coarse-grained' approach gives a high-level overview of what genes and proteins do and who they do it with.

However, scientists need to focus in greater detail to find out the particular parts of multi-functional proteins responsible for specific interactions, or to identify the functions that will be impacted by a specific mutation.

Conway postdoctoral research fellow, Dr Colm J. Ryan from UCD School of Medicine & Medical Science along with colleagues in the University of California, San Francisco reviewed the 'fine-grained' techniques that seek to address this gap in a recently published article in *Nature Reviews Genetics*.

Dr Ryan, first author on the publication, said, "The work set out to review computational and experimental advances that allow us to identify both the parts of proteins responsible for mediating specific interactions and the functional consequences of specific mutations.

These functional consequences include altered sensitivities to different drugs, and increased dependencies on the functions of other genes."

Ultimately, methods such as those discussed in the review may lead to the development of improved targeted therapeutics. For example, it has been observed in cancer that different mutations of the same oncogene can result in different clinical outcomes, including differential sensitivities to therapeutics. Such phenomena are poorly understood, and drug-gene and gene-gene interaction screens of the type discussed in the paper will be necessary to address this gap in our knowledge.

More information: High-resolution network biology: connecting sequence with function. Colm J. Ryan, Peter Cimermančič, Zachary A. Szpiech, Andrej Sali, Ryan D. Hernandez & Nevan J. Krogan. *Nature Reviews Genetics* 14, 865–879 (2013) [DOI: 10.1038/nrg3574](https://doi.org/10.1038/nrg3574)

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