

You are the company you keep—A new screening method detects direct biomolecule interactions

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Proteins are the building blocks of the cell. They do most of the work and are essential for the structure, function and dynamic regulation of the cell and body's tissues and organs. Proteins rarely work alone, they interact, form protein complexes or bind DNA and RNA to control what a cell does. These complexes are key pieces of many important reactions within the cell, such as energy metabolism or gene regulation. Any



change in those interactions, which can for example be caused by a mutation, can make the difference between health and disease. Hence, for understanding how cells operate, or what might go wrong in ill cells, it is essential to know how their building blocks interact.

New technologies allowed scientists during the last decades to understand the genetic information an organism possess, which of this information is actively used and which proteins are made by the cell in different circumstances. Now it is a big challenge to understand how biomolecules such as proteins and RNA messenger molecules combine to form the complexes required for a functional cell. In other words, we know the ten thousands of parts a cell is build off, but we don't know how they belong together.

In a paper published in *Nature Communications*, scientists at the Centre for Genomic Regulation (CRG) describe the development of a new method, named "rec-YnH", which was designed to understand the complexes formed between hundreds of proteins and RNAs at the same time.

The method, whose development was led by Sebastian Maurer in collaboration with the Luis Serrano laboratory, is the first technique that allows the detection of interactions between a large number of proteins and RNA molecules at the same time. The researchers put emphasis on the development of a doable and affordable method which is widely applicable.

"Our method reliably measures interactions between many proteins or many proteins and RNA fragments without the need for expensive, specialized equipment," explains Sebastian Maurer. "This methodology can be used by any standard biomedical research laboratory and will be useful for studying a particular process in the cell but also for researchers having to explore millions of protein interactions at a time to



look for a complex involved in a particular disease," he concludes.

Two CRG laboratories successfully combined their expertise in bioinformatics, biochemistry and molecular biology to implement and validate the method. "Our collaboration resulted in an affordable and feasible method that produces high-quality maps of protein-protein and protein-RNA interactions", says Jae-Seong Yang, postdoctoral researcher and co-first author of the paper.

"Interactions between proteins and RNA are key for many biological processes including gene regulation, and our method is the first that can detect interactions between hundreds of proteins and RNAs at the same time. Having such an efficient new tool at hand will be extremely helpful to answer important questions related to many diseases," states co-first author of the study and CRG researcher Mireia Garriga.

More information: Jae-Seong Yang et al, rec-YnH enables simultaneous many-by-many detection of direct protein–protein and protein–RNA interactions, *Nature Communications* (2018). DOI: 10.1038/s41467-018-06128-x

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