Scientists test commonly used antibodies

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If a strand of your DNA was stretched out completely, it would be more than six feet long. It's hard to imagine that it can fit inside the nucleus of one of your cells, but that's exactly how it works.

For much of the last century, scientists have been busy figuring out how DNA is packaged in cells, and have found strong indications that the packaging is integral to how DNA works. The packaging – comprised mostly of an amino acid molecule called a histone – influences the on and off switches of different genes that regulate cellular function and play a role in human diseases ranging from cancer to genetic disorders. Scientists study histones by using antibodies to specific "flavors" of histones that are only very slightly different from one another. The antibodies help to pinpoint what DNA is being packaged by a certain kind of "flavor" of histone, and how that affects gene regulation. Different flavors affect genes differently.

"And this is where it gets complicated," says Jason Lieb, PhD, who led the project. "Many companies make these antibodies that we scientists use in our labs – but there are so many different kinds of histones and types of tests we do that it's just not feasible for the companies to anticipate every single way that a given antibody can be used."

This is a problem, explains Lieb, who is a professor of biology at UNC-Chapel Hill and member of UNC Lineberger Comprehensive Cancer Center, since scientists can't be absolutely certain that the antibody is recognizing a specific "flavor" of histone, or one that is very closely related.

"Histones are essentially the key to the DNA library. They tell you which 'shelves' of that library – or areas of the genome – are open or closed to information moving in and out. But since the differences between the different 'flavors' of histones are often extremely small, and it's likely that an antibody may react with more than one histone or in different ways depending on the type of test being used in the lab. It makes scientific precision very difficult," Lieb notes.

In a paper published today in the journal Nature Structural and Molecular Biology, Lieb and his colleagues from across the country describe how they tested more than 200 antibodies against 57 histone modifications (or flavors) in three different organisms, using three different tests commonly used in this kind of genetic analysis. They found that about 25 percent of antibodies currently sold have a problem with specificity – targeting the anticipated histone – in a given test. They believe that this proportion is likely to remain steady over time.

"So we thought, ok, we need to help ourselves as scientists. We set up a web-based searchable database at http://compbio.med.harvard.edu/antibodies. Our results are there and other scientists can also post their results so that we have a self-sustaining, up-to-date source of information that is really important to scientists working to understand a broad range of genetic phenomena," he said.

More information: www.nature.com/nsmb/index.html

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