Study reveals more about how immune cells create new types of antibodies

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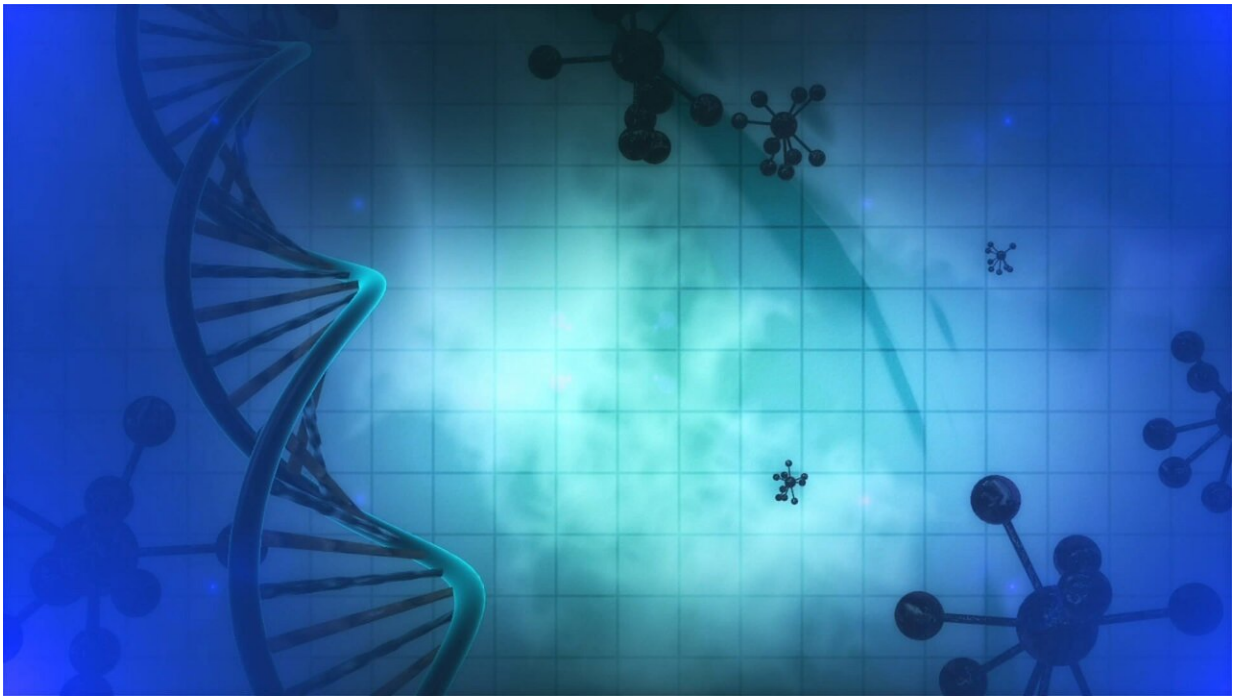

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A team of researchers at Boston Children's Hospital has learned more about the process of V(D)J recombination and how it makes use of chromatin looping to collect segments that are to be spliced. In their paper published in the journal *Nature*, the researchers outline their research and what they learned about the ways immune cells match bits of genetic code to create new types of antibodies. Ferenc Livak and

André Nussenzweig with NIH have published a News & Views piece outlining the work done by the team in the same journal issue.

As the researchers note, much work has gone into learning how the human immune system works. One finding is that immune cells have a way of mixing and matching bits of genetic code to create new antibodies when new threats are discovered. But until now, this mixing and matching process has been somewhat of a mystery. In this new effort, the researchers set out to learn more about how it works.

The researchers started with the knowledge that a process called V(D)J recombination allows the immune system to generate new antibodies. They also point out that DNA strands are packaged with proteins into chromatin—and each package has multiple loops. When the body detects a new threat, the loops in the chromatin move distant DNA segments closer together.

The work by the team in Boston showed how B cells exploit loop formation to create new antibodies. They found that RAG enzymes couple with mechanisms that take part in setting off the first step of V(D)J recombination—they force the D and J to join. Next, as loops are formed, DNA moves past the RAG complexes. Meanwhile, other factors impede extrusion, which pauses the DNA movement, allowing the RAG access. This allows for presenting gene substrate segments to the RAG complex for V(D)J recombination. The team also found that a protein called cohesin is involved in running the loop extrusion/RAG process. They note also that while their work was centered on the V(D)J recombination process, they believe their findings will have implications for other processes involved in gene regulation.

More information: Xuefei Zhang et al. Fundamental roles of chromatin loop extrusion in antibody class switching, *Nature* (2019). DOI: 10.1038/s41586-019-1723-0