MeCP2: A binding protein that prevents DNA from being wrapped up in nucleosomes

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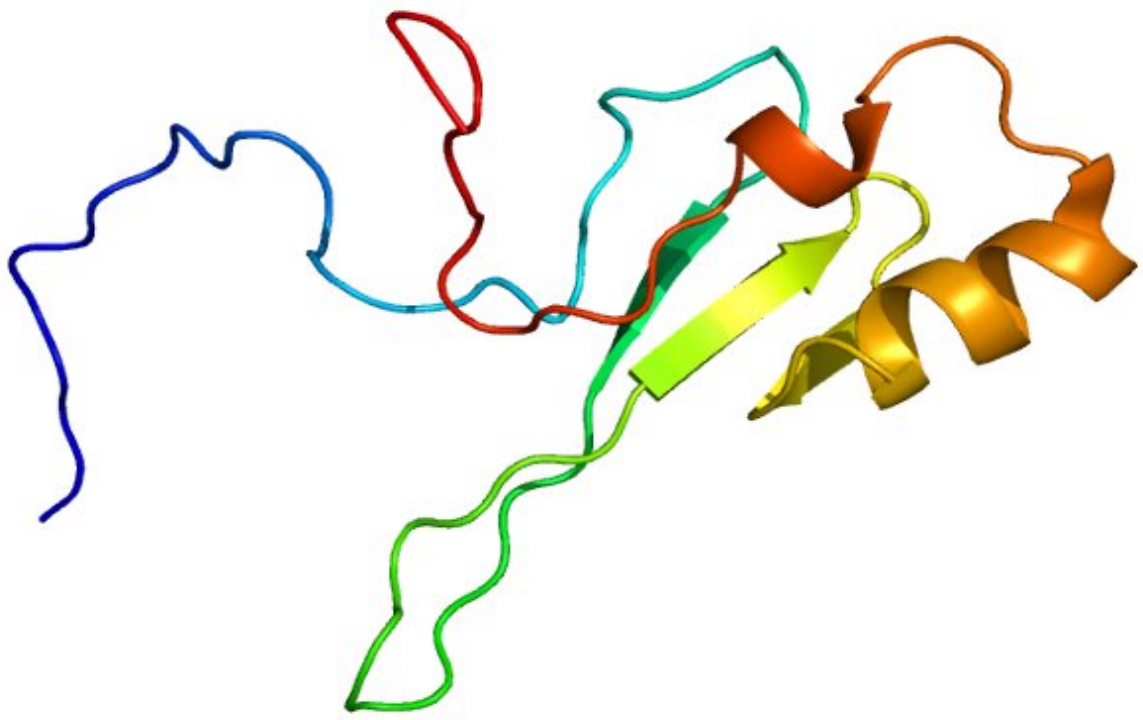

Structure of the MECP2 protein. Based on PyMOL rendering of PDB 1qk9. Credit: CC3.0 Emw

A team of researchers working at the Institute of Genetics and Molecular and Cellular Biology in Illkirch, France, has found that the MeCP2 protein binds to DNA in a way that prevents it from being wrapped up in

nucleosomes. In their paper published in the journal *Science*, the group describes their study of different kinds of cytosines and adenosine repeats in DNA and how they discovered what could turn out to be a molecular clue about the origin of Rett syndrome. Jian Zhou and Huda Zoghbi with the Jan and Dan Duncan Neurological Research Institute in Houston, Texas, have published a Perspective piece on the work done by the team in France, in the same journal issue.

Rett syndrome is a genetic disorder that most often affects girls—symptoms typically begin soon after their first birthday as neurological function begins to deteriorate. There is no cure, though there are medications that can reduce symptoms. Twelve years ago, researchers discovered that the syndrome was caused by mutations in DNA that code for a protein called MeCP2. Until now, it was not known what sort of problems with the MeCP2 protein led to Rett syndrome.

In this new effort, the researchers were studying different kinds of cytosines and adenosine repeats in DNA—they wanted to learn more about the role some proteins play when they bind to parts of DNA strands and how they impact the regulation of those genes. In so doing, they discovered that MeCP2 binds certain repeating sequences in strands of DNA.

Taking a closer look using X-ray crystallography, the researchers found that MeCP2 with unmutated genes changed the structure of the DNA slightly in a way that kept the DNA from being wrapped in nucleosomes. In sharp contrast, in cases with Rett-related mutations, there was no such binding and thus no alteration of the DNA—and because of that, the DNA became wrapped up with nucleosomes. The researchers have not yet tested whether the presence of the extra nucleosomes changes the regulation of the affected genes. If that turns out to be the case, then it would mark a breakthrough in better understanding the origins of Rett syndrome.

More information: Abdulkhaleg Ibrahim et al, MeCP2 is a microsatellite binding protein that protects CA repeats from nucleosome invasion, *Science* (2021). DOI: 10.1126/science.abd5581

Jian Zhou et al, Repeat after Me(CP2)!, *Science* (2021). DOI: 10.1126/science.abj5027