**TOOLBOX**

# DNA typo tracker uncovers glitches in gene regulation

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A new tool allows researchers to identify thousands of genome errors in dozens of people at once, a huge boost in efficiency from previous methods[1].

The technique is a variation on so-called **ChIP-Seq**, which detects segments of DNA that serve as landing strips for proteins that control gene expression. It allows researchers to home in on three times as many of these landing strips as they previously could, and in a fraction of the time. It also pinpoints variants that deter regulatory proteins from touching down on the DNA, and that may be associated with conditions such as autism.

Large genomic studies have identified many of these variants, but offer few clues to their function. The new work uncovers interactions between genetic sequences and regulatory proteins, hinting at the variants' roles in gene expression. The work appeared in April in *Cell*.

Scientists perform ChIP-Seq by growing cells in a tube, breaking them open to release DNA and then using antibodies as 'molecular magnets' to pull out stretches of the genome bound to proteins. They then sequence those regions to see **how they differ** between individuals with and without a condition such as autism.

But scientists had to perform these analyses on one genome at a time, and normal variations between individuals can mask genetic variants associated with a condition. The assays are also expensive and time-consuming, limiting the number of samples that researchers can analyze.

## Binding interrupted:

The new method sidesteps these limitations by pooling genetic samples from a group of people and performing ChIP-Seq on the pooled DNA. If an individual in the group carries a mutation that disrupts a landing zone — preventing or impeding the protein's binding — the mutated strip should

be underrepresented in the extracted pool of molecules.

The researchers tested their technique on cell lines from 60 unrelated people, using antibodies to pull out five regulatory proteins that control immune cell development. They then counted the number of copies of each piece of DNA bound to each of those proteins.

Up to 3 percent of the extracted DNA-protein pieces was underrepresented in the pool of molecules. The researchers identified errors in the DNA segments that may prevent one or more regulatory proteins from binding.

Comparing the binding sites with those identified in a previous ChIP-Seq study, the researchers found a near-perfect overlap, confirming the new method's accuracy[2].

**REFERENCES:**

1. Tehranchi A.K. *et al. Cell* **165**, 730-741 (2016) **PubMed**
2. Waszak S.M. *et al. Cell* **162**, 1039–1050 (2015) **PubMed**