GENE REGULATION

Transcription factors come to call

By fusing transcription factors (TFs) to a protein that recruits bar-coded transposons, researchers can identify genomic sites visited by these DNA-binding proteins.

When it comes to TFs and promoters, most people want to know all the promoters targeted by their particular TF. Not so for a group of researchers from Washington University—Haoyi Wang, Mark Johnston and Robi Mitra were interested in the opposite, namely identifying all the TFs that bind a particular promoter.

Figure 1 | Calling cards for TFs Image courtesy of Mark Johnston and Laura Kyro.

Their idea was to equip TFs with calling cards these proteins would leave at every promoter they visit, after which they would simply collect and read the cards (**Fig. 1**).

The group developed a system in yeast in which they fuse TFs to a protein that recruits a transposon that inserts close to the TF binding site. The transposon carries a DNA sequence bar code that is matched to the TF, and thus becomes the TF's 'calling card'. By pooling cells transfected with different TFs and retrieving the bar codes together with adjacent genomic DNA, they can identify every TF that visited a particular location.

As proof-of-principle, they fused the Gal4 DNA binding domain to Sir4, which recruits the Ty5 transposon, and analyzed the inserted bar codes by PCR or on a DNA microarray. The initial results were encouraging, but Mitra sees this only as the first step. "The real strength of the method," he says, "is the genome-wide analysis of a large number of TFs, all in one experiment; but for that we need to couple it to next-generation sequencing."

Once high-throughput sequencing is in place, the group wants to apply the method to a mammalian system. But even in yeast the integration efficiency of the transposons is relatively low and modifications to make it better, such as using a different transposon or targeting mechanism, will be needed.

Such a system will have one distinct advantage over other tools that analyze TF-promoter interactions: it will provide a history of the binding of each TF. In a transgenic mouse expressing a TF and a bar-coded transposon, analysis of the integration sites will yield all the sites the TF visited during development.

Science fiction? For the moment, but let us talk again a year from now.

Nicole Rusk

RESEARCH PAPERS
Wang, H. *et al.* Calling cards for DNA-binding proteins. *Genome Res.* **17**, 1202–1209 (2007).