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Cover In this issue, the complexity of the evolutionary relationship between transcription factor (TF) binding and transcriptional output in mammals is explored in a study of three TFs (represented by switches) from four closely related mice. Here, they are depicted as trying to work out the complex interconnections (wires) between the switches and turning on the light bulb (i.e., the transcriptional output via gene expression). (Cover illustration by Spencer Phillips is based on a concept by Mary Bergman; both are at the European Bioinformatics Institute [EMBL-EBI]. © EMBL. [For details, see Wong et al., pp. 167–178.]