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Single-molecule imaging uncover novel pathways in transcriptional regulation

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Metalloregulators regulate transcription in response to metal ions. Many studies have provided insights into how transcription is activated upon metal binding by MerR-family metalloregulators. In contrast, how transcription is turned off after activation is unclear. Turning off transcription promptly is important, however, as the cells would not want to continue expressing metal resistance genes and thus waste energy after metal stress is relieved. Using single-molecule FRET measurements, we studied the dynamic interactions of CueR, a Cu+-responsive MerR-family metalloregulator, with DNA. We discovered that a CueR molecule coming from solution can directly substitute for a DNA-bound CueR or assist the dissociation of the incumbent CueR. The kinetics of the direct protein substitution and assisted dissociation reactions indicate that these two novel processes can provide efficient pathways to replace a DNA-bound holo-CueR with apo-CueR, thus turning off transcription promptly and facilely. Using single-molecule tracking experiments, we further show that these novel pathways also operate in living bacterial cells.

[1] *C. P. Joshi, D. Panda, D. J. Martell, N. M. Andoy, T.-Y. Chen, A. Gaballa, J. D. Helmann, P. Chen, Proc. Natl. Acad. Sci. USA 2012, 109, 15121-15126*

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