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GENE REGULATION

Tracking through time and nuclear space

A new single-molecule imaging assay has been developed to visualize the spatiotemporal dynamics of transcription factors in the nucleus. By detecting the rapid diffusion of proteins across the eukaryotic nuclear space, this new tracking procedure is capable of identifying the different ways by which transcription factors seek out their binding sites.

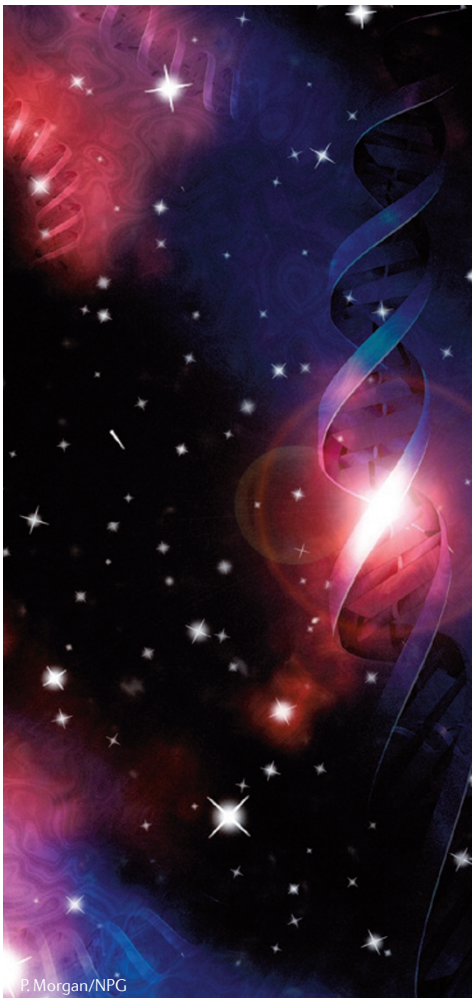
The researchers adapted the photoactivated localization microscopy (PALM) assay for single-molecule detection in the nucleus of human osteosarcoma cells to follow the movement of two distinct transcription factors: c-MYC and positive transcription elongation factor (P-TEFb). c-MYC is known to bind directly to DNA, whereas P-TEFb binds to the transcription machinery.

Notably, the technique was able to show the different strategies used by c-MYC and P-TEFb to 'explore' the nuclear space. c-MYC showed free diffusion in three-dimensional space and binds with equal probability to any target in the nucleoplasm. P-TEFb exploration was more constrained to specific routes: it was guided by nuclear structures that led to spatiotemporal correlations between binding events.This more regulated mechanism for P-TEFb movement could have strong implications in our understanding of how molecular complexes assemble.

Importantly, this work confirms that the nuclear space is transversed in a protein-specific manner. Future work using this method could further elucidate the strategies of other transcription factors in searching for their target binding sites.

Bryony Jones

> "the nuclear space is transversed in a protein-specific manner"



P. Morgan/NPG

ORIGINAL RESEARCH PAPER Izeddin, I. *et al.* Single-molecule tracking in live cells reveals distinct target-search strategies of transcription factors in the nucleus. *eLife* http://dx.doi.org/10.7554/eLife.02230 (2014)

WEB SITE

Xavier Darzacq's web site: http://mcb.berkeley.edu/index.php?option=com_mcbfaculty&name=darzacqx