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TECHNIQUE

Lights on gene expression

Writing in *Nature Methods*, Wang *et al.* describe a new technique to spatiotemporally manipulate gene expression with a synthetic, light-inducible activator of transcription.

To achive light-inducible gene expression, the authors made use of the small photosensitive protein vivid (VVD). VVD contains a light, oxygen or voltage (LOV) domain, which dimerizes in response to blue light. VVD was coupled to a fragment of the transcription factor Gal4 termed Gal4(65), which comprised a DNA-binding domain but lacked a dimerization domain and, thus, was unable to bind its cognate DNA sequence. Following fusion of Gal4(65) with VVD, light-controlled LOV dimerization allowed Gal4(65) dimerization and DNA binding. Next, the transactivation domain of the transcription factor p65 was added to the Gal4(65)–VVD construct to generate a synthetic protein (termed GAVPO) that can be induced by blue light to initiate transcription of genes containing Gal4-binding sites in their promoter region. This transactivator–promoter transgene system was named LightOn.

In vitro studies showed that the level of gene expression induced by the LightOn system was comparable to that driven by the human cytomegalovirus (HCMV) early promoter. LightOn-regulated genes could be activated by both continuous illumination and repeated short light pulses. Moreover, the kinetics of LightOn-controlled gene expression depended on the strength and duration of cell illumination, with 30 minutes of illumination being sufficient for the expression of a reporter protein. Interestingly, the half-life of the activated GAVPO was estimated to be 2 hours, which allows tight temporal control of gene expression.

Further analysis showed that the LightOn transgene system can be used to spatiotemporally control gene expression in mice; a GAVPO vector and a Gal4-binding reporter vector were transfected into the livers of mice, and the reporter protein could be traced following exposure of mice to illumination. In addition, more localized gene expression could be achieved with the use of optical fibres. Finally, in a preliminary disease model, regulation of LightOn-controlled insulin expression by blue light illumination successfully reduced blood glucose levels in diabetic mice.

Based on their findings, the authors suggest that the fast kinetics, high transcriptional activity and reversibility of the LightOn gene expression system render it a powerful tool.

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ORIGINAL RESEARCH PAPER Wang, X., Chen, X. & Yang, Y. Spatiotemporal control of gene expression by a light-switchable transgene system. *Nature Methods* **9**, 266–269 (2012)

LightOn print on a cell monolayer through light-controlled expression of mCherry. Image courtesy of Yi Yang, East China University of Science and Technology, Shanghai, China.