RECOMMENDED READING

The development and application of CRISPRi and CRISPRa technologies

Introduction

CRISPR activation (CRISPRa) and CRISPR interference (CRISPRi) are powerful, emerging tools for the targeted modulation of gene expression. The following publications document the development and application of these technologies.

CRISPRi

1. Gasperini, M., Hill, A. J., McFaline-Figueroa, J. L., Martin, B., Kim, S., Zhang, M. D., Jackson, D., Leith, A., Schreiber, J., Noble, W. S., Trapnell, C., Ahituv, N., & Shendure, J. (2019). A genome-wide framework for mapping gene regulation via cellular genetic screens. *Cell,* **176(6)**, 1516.

2. Yeo, N. C., Chavez, A., Lance-Byrne, A., Chan, Y., Menn, D., Milanova, D., Kuo, C.-C., Guo, X., Sharma, S., Tung, A., Cecchi, R. J., Tuttle, M., Pradhan, S., Lim, E. T., Davidsohn, N., Ebrahimkhani, M. R., Collins, J. J., Lewis, N. E., Kiani, S., & Church, G. M. (2018). An enhanced CRISPR repressor for targeted mammalian gene regulation. *Nature Methods,* **15(8)**, 611–616.

3. Liu, S. J., Horlbeck, M. A., Cho, S. W., Birk, H. S., Malatesta, M., He, D., Attenello, F. J., Villalta, J. E., Cho, M. Y., Chen, Y., Mandegar, M. A., Olvera, M. P., Gilbert, L. A., Conklin, B. R., Chang, H. Y., Weissman, J. S., & Lim, D. A. (2017). CRISPRi-based genome-scale identification of functional long noncoding RNA loci in human cells. *Science,* **355(6320)**, eaah7111.

4. Horlbeck, M. A., Gilbert, L. A., Villalta, J. E., Adamson, B., Pak, R. A., Chen, Y., Fields, A. P., Park, C. Y., Corn, J. E., Kampmann, M., & Weissman, J. S. (2016). Compact and highly active next-generation libraries for CRISPR-mediated gene repression and activation. *ELife,* **5**, e19760.

5. Gilbert, L. A., Horlbeck, M. A., Adamson, B., Villalta, J. E., Chen, Y., Whitehead, E. H., Guimaraes, C., Panning, B., Ploegh, H. L., Bassik, M. C., Qi, L. S., Kampmann, M., & Weissman, J. S. (2014). Genome-scale CRISPR-mediated control of gene repression and activation. *Cell,* **159(3)**, 647–661.

6. Gilbert, L. A., Larson, M. H., Morsut, L., Liu, Z., Brar, G. A., Torres, S. E., Stern-Ginossar, N., Brandman, O., Whitehead, E. H., Doudna, J. A., Lim, W. A., Weissman, J. S., & Qi, L. S. (2013). CRISPR-mediated modular RNA-guided regulation of transcription in eukaryotes. *Cell,* **154(2)**, 442–451.

CRISPRa

1. Weltner, J., Balboa, D., Katayama, S., Bespalov, M., Krjutškov, K., Jouhilahti, E.-M., Trokovic, R., Kere, J., & Otonkoski, T. (2018). Human pluripotent reprogramming with CRISPR activators. *Nature Communications,* **9(1)**, 2643.

2. Bester, A. C., Lee, J. D., Chavez, A., Lee, Y.-R., Nachmani, D., Vora, S., Victor, J., Sauvageau, M., Monteleone, E., Rinn, J. L., Provero, P., Church, G. M., Clohessy, J. G., & Pandolfi, P. P. (2018). An integrated genome-wide CRISPRa approach to functionalize lncRNAs in drug resistance. *Cell,* **173(3)**, 649-664.e20.

3. Simeonov, D. R., Gowen, B. G., Boontanrart, M., Roth, T. L., Gagnon, J. D., Mumbach, M. R., Satpathy, A. T., Lee, Y., Bray, N. L., Chan, A. Y., Lituiev, D. S., Nguyen, M. L., Gate, R. E., Subramaniam, M., Li, Z., Woo, J. M., Mitros, T., Ray, G. J., Curie, G. L., … Marson, A. (2017). Discovery of stimulation-responsive immune enhancers with CRISPR activation. *Nature,* **549(7670)**, 111–115.

4. Konermann, S., Brigham, M. D., Trevino, A. E., Joung, J., Abudayyeh, O. O., Barcena, C., Hsu, P. D., Habib, N., Gootenberg, J. S., Nishimasu, H., Nureki, O., & Zhang, F. (2015). Genome-scale transcriptional activation by an engineered CRISPR-Cas9 complex. *Nature,* **517(7536)**, 583–588.

5. Kiani, S., Chavez, A., Tuttle, M., Hall, R. N., Chari, R., Ter-Ovanesyan, D., Qian, J., Pruitt, B. W., Beal, J., Vora, S., Buchthal, J., Kowal, E. J. K., Ebrahimkhani, M. R., Collins, J. J., Weiss, R., & Church, G. (2015). Cas9 gRNA engineering for genome editing, activation and repression. *Nature Methods,* **12(11)**, 1051–1054.

6. Maeder, M. L., Linder, S. J., Cascio, V. M., Fu, Y., Ho, Q. H., & Joung, J. K. (2013). CRISPR RNA–guided activation of endogenous human genes. *Nature Methods,* **10(10)**, 977–979.

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