











## Computational design of a modular protein sense-response system

Anum A. Glasgow, Yao-Ming Huang, Daniel J. Mandell, Michael Thompson, Ryan Ritterson, Amanda L. Loshbaugh, Jenna Pellegrino, Cody Krivacic, Roland A. Pache, Kyle A. Barlow, Noah Ollikainen, Deborah Jeon, Mark J. S. Kelly, James S. Fraser and Tanja Kortemme

*Science* **366** (6468), 1024-1028.  
DOI: 10.1126/science.aax8780

### Sense and respond

Many signaling pathways start with cellular proteins sensing and responding to small molecules. Despite advances in protein design, creating a protein-based sense-and-respond system remains challenging. Glasgow *et al.* designed binding sites at the interface of protein heterodimers (see the Perspective by Chica). By fusing each monomer to one half of a split reporter, they linked ligand-driven dimerization to the reporter output. The computational design strategy provides a generalizable approach to create synthetic sensing systems with different outputs.

*Science*, this issue p. 1024; see also p. 952

#### ARTICLE TOOLS

<http://science.sciencemag.org/content/366/6468/1024>

#### SUPPLEMENTARY MATERIALS

<http://science.sciencemag.org/content/suppl/2019/11/20/366.6468.1024.DC1>

#### RELATED CONTENT

<http://science.sciencemag.org/content/sci/366/6468/952.full>

#### REFERENCES

This article cites 72 articles, 12 of which you can access for free  
<http://science.sciencemag.org/content/366/6468/1024#BIBL>

#### PERMISSIONS

<http://www.sciencemag.org/help/reprints-and-permissions>

Use of this article is subject to the [Terms of Service](#)

*Science* (print ISSN 0036-8075; online ISSN 1095-9203) is published by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. The title *Science* is a registered trademark of AAAS.

Copyright © 2019 The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works