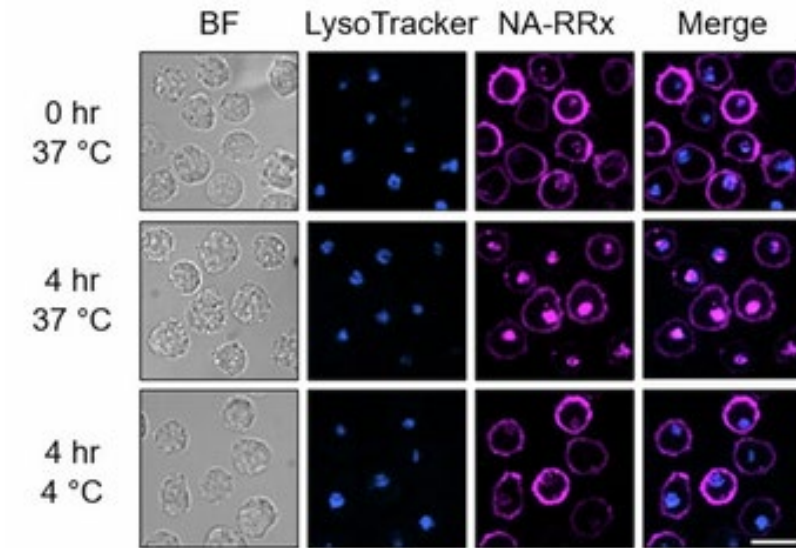


SMART Protein Splicing Enables Programmable Cell Surfaces



K562 cells engineered to display HER2 and EGFR proteins were treated with the SMART-SpyCatcher system and a biotin-labeled SpyTag. After adding a fluorescent probe (magenta), cells were imaged immediately or after incubation. Nuclei are shown in blue (Hoechst) and lysosomes in cyan (LysoTracker). Scale bar, 20 μ m.

Christian Kofoed, Girum Erkalo, Nicholas E. S. Tay, Xuanjia Ye, Yutong Lin, Tom W. Muir, Programmable protein ligation on cell surfaces. *Nature* 645, 793–800 (2025).
<https://doi.org/10.1038/s41586-025-09287-2>

Work was performed in part at NSLS-II

Scientific Achievement

A new splicing tool enables scientists to build custom proteins directly on cell surfaces programmed to activate when predetermined combinations of surface proteins are present.

Significance and Impact

This work could lead to therapeutics and diagnostics that are more specifically targeted toward specific cells or proteins of interest.

Research Details

- The “Splicing-Modulated Actuation upon Recognition of Targets” (SMART) system acts like a molecular logic gate on living cells.
- SMART can “read” combinations of surface protein markers and only activate when the correct combination is found.
- High resolution diffraction data were collected at the AMX beamline at NSLS-II, providing key information on biological structure.