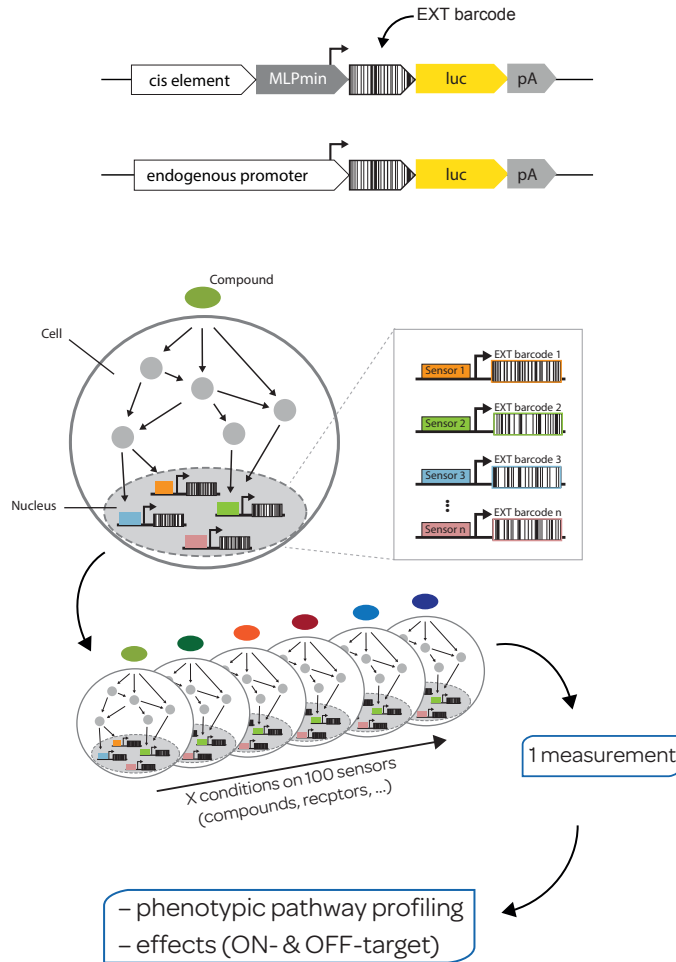


Assay principle

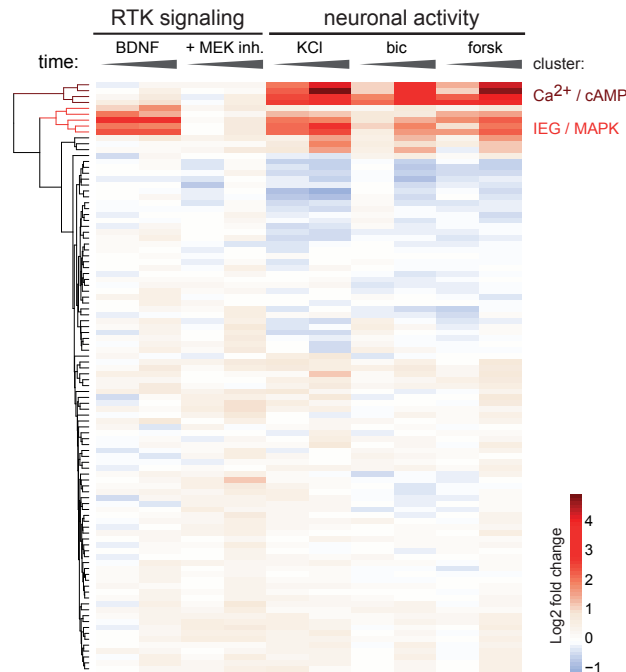
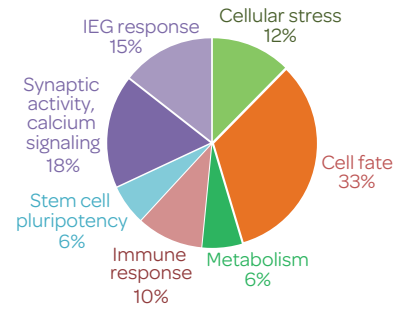
Genetically encoded pathway sensors are linked to EXT barcodes and luciferase. Sensors either consist of cis elements binding single transcription factors, or promoters of pathway-indicative genes.



Activated transcription factors serve as distal endpoints of signaling activities and bind to multiple pathway sensors coupled to barcoded EXT reporters. Network activity is deconvoluted via the cisPROFILER library in a multiplexed fashion using the EXT assay technology.

Signaling categories and benchmarking

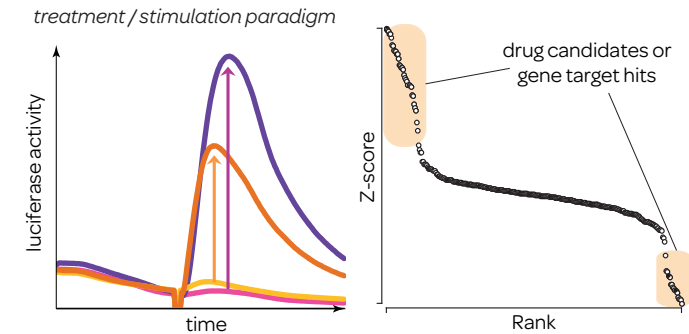
More than 100 distinct disease-relevant and customizable biosensors measure 20 different cellular pathways in 7 major biological categories.



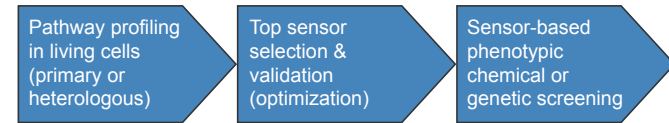
Primary mouse neurons were infected with cisPROFILER-containing AAVs. The RTK TrkB was stimulated by BDNF (MEK inhibitor as specificity control), neuronal activity was induced by KCl (depolarization), bicuculline (bic, GABA antagonist), or forskolin (forsk, cAMP agonist). Sensors were identified that discern between RTK and neuronal activity, with the potential for specific drug development.

From sensor validation to screening

Top sensors are validated in live-cell or endpoint experiments, and can be used for compound or genetic screening purposes.



Summary



Benefits

- ✔ Transient transfection or viral delivery of cisPROFILER library (suitable for large variety of heterologous and primary cells)
- ✔ Highly sensitive, specific & robust sensor performances (biological and internal EXT replicates, calibrators)
- ✔ True multiplexing by NGS readout (multiple pathway activities profiled simultaneously)
- ✔ Strong time- and cost-saving opportunities (generates large amount of data in one measurement)
- ✔ Each biosensor available as single luciferase assay (HTS compatibility of identified top sensor)