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A live-cell sensor for cyclin-dependent kinase 2 activity

Scientists in Dr. Tobias Meyer's lab at Stanford have developed a live-cell fluorescent sensor for cyclin-dependent kinase 2 (CDK2) activity. Cellular transitions from proliferation to quiescence and quiescence to proliferation are important both during development and for normal adult physiology. Proliferation is characterized by progression through the cell cycle, which is driven by CDK activity. The cell cycle is typically studied in synchronized cells using biochemical approaches, which has several drawbacks including loss of single cell information and the potential for synchronization procedures to trigger stress responses in cells. To overcome these limitations, the inventors have developed the first live-cell sensor for CDK2 activity. Because CDK2 activity is tightly coupled to progression through the cell cycle, the sensor also detects whether cells are in a proliferative or quiescent state.

Stage of research
Using *in vitro* kinase assays and specific inhibitors, the inventors confirmed the sensor responds rapidly and specifically to CDK2 activity. In addition, using time-lapse microscopy and customized cell tracking they showed the senor has a dynamic range well-suited to monitor changes in CDK2 activity throughout the cell cycle.

Applications

- Drug screening- identify compounds that:
  - Promote proliferation (for regenerative medicine)
  - Promote quiescence (for cancer therapy)
- Research
  - Cell cycle studies
  - Determine if cells are in a proliferative or quiescent state

Advantages

- Only live-cell CDK2 activity sensor
- Monitor CDK2 activity instantaneously in real-time
- Genetically encoded and can be transduced into any cell type using a virus
- Uses only 1 fluorescent channel
- High signal-to-noise ratio
- Provides molecular timer for progression through interphase
- Can determine a cell's commitment to the cell cycle without need to perturb it or monitor its future behavior.

Publications

- Spencer SL, Cappell SD, Tsai FC, Overton KW, Wang CL, Meyer T. The proliferation-quiescence decision is controlled by a bifurcation in CDK2 activity at mitotic exit. Cell. 2013 Oct 10;155(2):369-83. doi: 10.1016/j.cell.2013.08.062. Epub 2013 Sep 26.

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