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Specific kinase biosensors to probe cancer metabolism

Substrate peptides for Ser/Thr kinases to investigate the metabolic processes of cancer cells.

Technology No. 20170295

IP Status: Issued US Patent; **Application #:** 15/926,640

Applications

- Clinical diagnostic to determine cancer behavior and optimal treatment strategy
- Oncology research on mechanism of resistance development in cancers (specifically leukemias)
- Chemotherapeutic drug identification and development
- Basic kinase research

Key Benefits & Differentiators

- **Assess activity of multiple kinases in real-time:** Kinase-specific substrates have the potential to be linked to various signal peptides to facilitate simultaneous monitoring of distinct kinases.
- **Use with wild-type, unmodified kinases:** Method does not require the modification or tagging of kinases prior to experimentation.
- **Simple readout amenable to high throughput optimization:** When combined with fluorescent signaling technologies, substrates can be developed for with multi-well plate readers.

Metabolic plasticity in cancers

Cancerous cells exhibit alterations to their metabolism that may contribute to proliferation, survival and the development of drug resistance to commonly prescribed cancer treatments. Unfortunately the mechanisms of these metabolic changes aren’t well understood, limiting progress on cancer drug therapies. Laurie Parker’s lab at the University of Minnesota developed four artificial, cell-permeable kinase substrates that serve as biosensors for serine/threonine kinases (LKB1, AMPK, mTOR and Akt) that are intimately involved in metabolism regulation. The ability to determine the activity of these critical kinases in normal, cancerous and drug-resistant cancer cells will help determine the metabolic activities of cells, how resistance develops, and provide molecular targets for therapeutic development.

Making sense of the kinases

The kinase-specific biosensors have the potential to be combined with assayable fluorophores or other signal moieties, or the phosphorylation of the peptidesalone can be measured using alternate methods such as mass spectrometry. Substrates can further be selected based on their ability to permeate the membrane and their compatibility with live cells, The capability of the sensors to provide real-time signaling facilitates the potential to simultaneously monitor distinct kinase activities in native cellular environments. The sensors are antibody independent, can be optimized for high-throughput screening methods and (unlike other approaches to monitoring kinase activity) do not need to be genetically encoded, making them ideal for development in diagnostic applications.

Phase of Development

Proof of concept. Substrate sequence motifs identified for the kinases LKB1, AMPK, mTOR and Akt and preliminary substrates for LKB1 and Akt.

Researchers

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External Link (cbs.umn.edu)

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