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Universal tyrosine kinase substrates

Non-selective, universal substrates for tyrosine kinases that couple with a fluorescent readout mechanism to serve as quantity and quality control (internally and/or between samples).

IP Status: US Patent Issued; **Issued Patent No.** 10,883,992

Applications

- Standardization and normalization of tyrosine kinase enzyme preparations
- Basic research and profiling of tyrosine kinases
- Therapeutic tyrosine kinase inhibitor identification and development (i.e. for acute myeloid leukemia)
- Diagnostic assay development

Key Benefits & Differentiators

- **Compare activity of any tyrosine kinases:** Developed substrates are efficiently phosphorylated by all tested tyrosine kinases, facilitates meaningful comparisons between batches of the same or different different tyrosine kinases.i
- **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 assays:** Phosphorylated substrate binds to terbium, creating a fluorescent signal measurable by multi-well plate readers.

The need for kinase controls

Due to their universal presence in cells, the ability to measure and compare the activity of kinases is critical for basic research and to develop drugs and diagnostics for a myriad of diseases. However, the variability in activity between different kinases or between batches of the same kinases has hampered the development of robust control/normalization techniques. Dr. Laurie Parker's lab used their previously developed KINATEST-ID platform to design and optimize a non-selective "universal" substrate for tyrosine kinases that can serve as a normalizer for any kinase of interest. This fully characterized standardizing compound allows for more accurate comparisons of activities from reaction to reaction for other substrates or inhibitors.

A universal tyrosine kinase substrate provides reliable comparisons

Currently the only identified universal tyrosine kinase substrate is the polyGlueTyr polymer, which is a relatively poor substrate with slow rates of phosphorylation. The newly developed substrate is efficiently phosphorylated by all tyrosine kinases tested and compatible with high-throughput screening methods. The substrate can be used as a "standardizer" for intrinsic activity, for quality control, and for normalization of kinase enzyme preparations in comparative experiments. Since the method does not require kinase modification or tagging of kinases, it can further serve as a real time baseline of total tyrosine kinase activity in living cells. When combined with biosensors for specific tyrosine kinases of interest, the approach facilitates monitoring specific kinase activities in their novel cellular environment over time. This technique

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Life Sciences/Diagnostics & Imaging
Life Sciences/Pharmaceuticals
Life Sciences/Research Tools

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can be applied to diagnostics and drug discovery methods that require monitoring of pharmacodynamics.

Phase of Development

In vitro testing with a variety of tyrosine kinases.

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

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Try

- Trial period is up to 12 months
- Trial fee is $6,000 for a 12 month period
- No US patent fees during Try period

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- $25,000 conversion fee (TRY to BUY)
- $5000 annual minimum credited against royalties thereafter
- Royalty rate of 3% (2% for MN company)
- Royalty free for first $1M in sales

Researchers

Laurie Parker, PhD
Associate Professor, Biochemistry, Molecular Biology and Biophysics
External Link (cbs.umn.edu)

Publications

In Silico Design and in Vitro Characterization of Universal Tyrosine Kinase Peptide Substrates
Biochemistry, 2018, 57, 12, 1847-1851