New Powerful Tool for Monitoring of Kinase Activity

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Technology description

Description

This technology is focused on the development of a powerful technology for the simultaneous monitoring of protein kinase activities in cell and tissue extracts using a multiplexed electrochemical assay. This simple chip-based approach will profile kinase activity in the presence and absence of kinase inhibitors, directly from the cellular solution. This electrochemical technique readily lends itself to miniaturization, automation, and multiplexing and will lead to production of biosensor and/or micro-array devices.

Background

In the cellular signaling network, many enzymes and receptors are activated (phosphorylated) or deactivated (dephosphorylated) by protein kinases. As a result of these modifications, the function of the protein may change. Many disease processes including cancer, heart disease, diabetes, autoimmune and chronic inflammatory diseases are the result of defects in the signal transduction pathways from abnormal protein phosphorylation. Because of the role of protein kinases in these diseases, pharmaceutical companies are intensively seeking drug candidates that can control or inhibit specific kinases in the signal transduction pathways.
Cost effective techniques used to identify and quantify protein phosphorylation or kinase activity are becoming increasingly important for the diagnosis and therapy of major diseases. New analytical methods that identify possible targets, assess kinase inhibitors and quantify protein kinase activity directly from complex cellular mixtures are critical for understanding the signaling pathways of these diseases.
Pharmacodiagnostics are tests to identify patients for therapy using pharmaceuticals or to monitor how well a specific pharmaceutical is working. In oncology, pharmacodiagnostics combines a specific anticancer drug (pharmaco-) with a specific diagnostic test (diagnostics) and thereby improves the treatment of cancer by preselecting suitable patients and monitoring the success of the therapy. Pharmacodiagnostics has the potential to uncover variability in drug response and to tailor individualized drug prescription so that the balance between efficacy and toxicity is optimized for every patient.

Application area

Diagnostic- kinase activity profiling for the early diagnosis of cancer and for monitoring its progression; Personalize drug treatments
Pharmacodiagnostics- monitoring the effectiveness of cancer drug treatment
Drug discovery- rapid and inexpensive method for screening kinase inhibitors
Current methods for the detection of protein phosphorylation rely on radio-labeled ATP, fluorescence-based methods, and fluorescence resonance energy transfer (FRET). However, these methods require additional modification of the peptides with an electro-active or optical label is, which increases the cost and causes tedious and time-consuming handling procedures.
In contrast, this electrochemical approach allows for the direct measurement of kinase activity and does not require post-labeling procedures and/or radio-labels. The assay described here is rapid, simple, safe, inexpensive, and sensitive.
This electrochemical method will provide an easy-to-use and low-cost alternative to the existing methods. Future work will provide key data about kinase-catalyzed phosphorylation reactions in vitro and inhibitor activities. It is anticipated that continued development of this technology will lead to miniaturized electrochemical devices and micro-arrays that will have important implications for drug discovery.

Institution

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