

QTL BIOSYSTEMS

Detection amplification technology for bioassays

INTRODUCTION

Announcing QTL Lightspeed β -Secretase™

The major constituent of senile plaques associated with Alzheimer's disease is the β -amyloid peptide, derived from the amyloid precursor protein (APP) by proteolytic cleavage. This cleavage occurs at the β and γ cleavage sites. Early biochemical characterization and inhibitor profiling have indicated that both β and γ cleaving enzymes (secretases) are probably aspartic proteinases, and are currently the most attractive targets for therapeutic intervention for Alzheimer's disease.

The QTL Lightspeed β -secretase assay combines high-sensitivity with high speed for screening potential inhibitors against β -secretase. The assay is based on QTL's patented "superquenching" technology (see sidebox).

The main features of this assay are:

- Excellent Sensitivity.....14fmol β -secretase in 60 min. assay
- Enhanced Speed.....171fmol β -secretase in 10 min. assay
- Ultra-low sample requirement.....10 μ l total reaction volume
- DMSO and MeOH tolerance.....10% DMSO with 70% residual enzyme activity 10% MeOH with less than 5% loss in activity

SIDE BOX

QTL Lightspeed™ Technology How it Works

The QTL technology is based on the original discovery that, for certain fluorescent polymers, it is possible to quench the fluorescence emission of individual polymers with extremely high selectivity. This "superquenching" could also be reversed, by constructing a new molecule called a "QTL" (Quencher-Tether-Ligand). The QTL molecule can bind to a receptor site on a biological agent, which restores the fluorescent emission of the associated polymer. In effect, the QTL system is a molecular light bulb with a fast yet specific 'switch' that turns it on.

The implementation to protease detection constitutes a flexible platform that allows rapid development of a library of screening assays using the QTL technology platform. The QTL polymers are coated onto a support (such as a microscopic plastic bead, or a glass micro-array). A direct assay results from proteolytic cleavage of the substrate, which is incorporated directly into the QTL molecule. A variable fluorescence signal is observed, with a brightness that varies in a quantitatively precise manner with addition of target enzyme.

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ASSAY DESCRIPTION

The QTL Lightspeed protease assay makes use of fluorescence-quenching protease substrates with a peptide sequence that recognizes the enzyme of interest separating the QTL fluorescent polymer from our proprietary molecular quenchers. Proteolytic cleavage of the peptide releases the quencher from the QTL polymer, resulting in a quantitative signal that increases with enzyme activity or reaction time. Inhibitors for the enzyme activity modulate this signal increase, which can be tuned over a variety of sensitivity ranges as desired by target sensitivity requirements.

DETECTION REQUIREMENTS

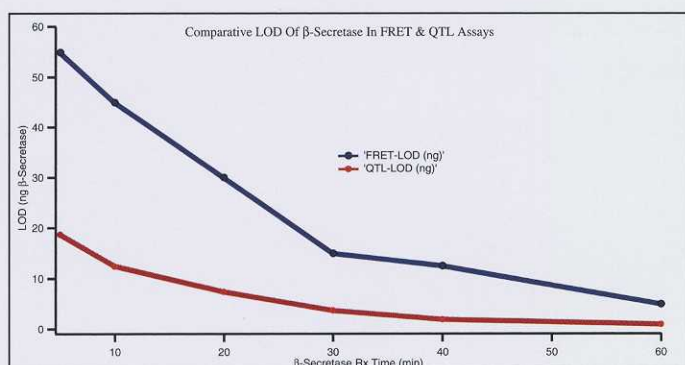
The QTL Lightspeed protease assay can be used in virtually all commercially-available fluorescence spectrometers and multi-well plate readers. The excitation (blue) and detection (green) wavelengths are compatible with all common fluorimeters. QTL technical personnel can assist with configuring the settings to optimize performance of the QTL Lightspeed assay.

TRADE-OFF POSSIBILITIES

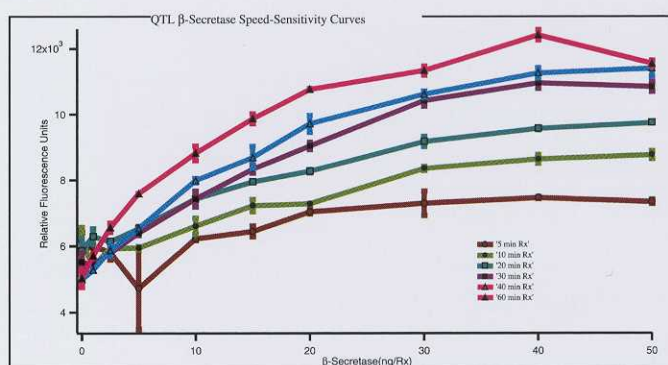
(Time Vs Sensitivity Vs Compound Requirement)

Because enzyme activity is catalytic, or based on the turnover of multiple chemical reactions with a single catalyst molecule, the increase in fluorescence in the QTL Lightspeed assay occurs more rapidly in the presence of larger concentrations of target enzyme. Because of this effect, a more sensitive assay platform allows the user to choose the optimal parameters for a particular screening assay. For example, if moderate sensitivity is required, the assay can be performed at much higher speed, where as much higher sensitivity can be achieved at moderate speed. The QTL Lightspeed β -secretase assay performs at least four times faster than competing assays at equivalent sensitivity.

Speed-sensitivity curves



Comparative LOD in FRET and QTL assays



Reagent availability

QTL Biosystems is launching a beta test program for this assay:
For information, email to: info@qtlbio.com