

## Announcing QTL Lightspeed $\beta$ -Secretase™

### Introduction

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

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

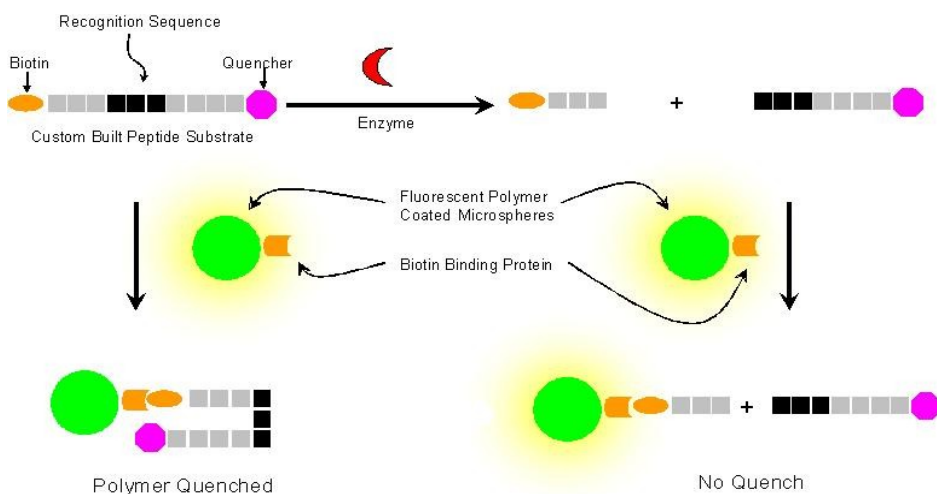
### The main features of this assay are:

- Excellent Sensitivity and Speed.....14 fmol  $\beta$ -secretase in 60 min. assay
- Supports multi well formats.....optimized for 96,384,1536 well plates
- Highly reliable.....CV < 4%, Z' factor > .7
- DMSO and MeOH tolerance.....10% DMSO with 70% residual enzyme activity

### SIDEBOX:

#### QTL Lightspeed™ Technology – How it Works (See diagram below)

- Detection system consists of a fluorescent polymer and quencher-tether-ligand (QTL) moieties
- The QTL moieties consist of a quencher that quenches polymer fluorescence, a ligand that is specifically cleaved by target enzyme, and a tether that connects the quencher and ligand
- When the reactive tether is cleaved by enzyme, the quencher is released from the polymer, resulting in a quantitative signal that increases with enzyme activity or duration of the assay
- Inhibitors of the enzyme modulate this signal increase, which can be tuned over a variety of sensitivity ranges as desired by target sensitivity requirements.



### Contact Info

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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

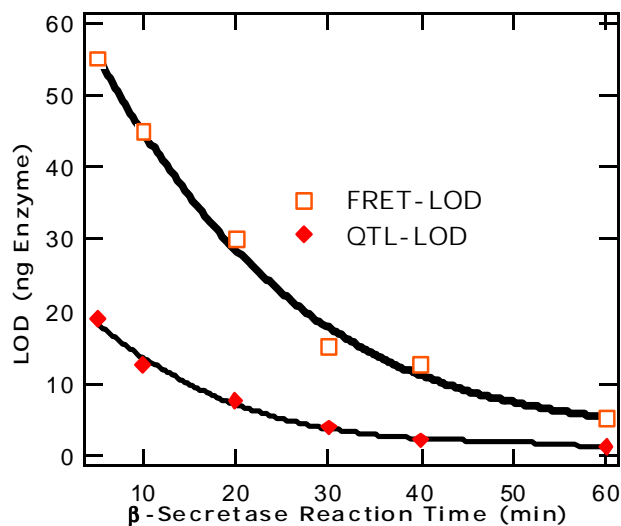
The QTL Lightspeed protease assay can be used in virtually all commercially-available fluorescence spectrometers and multi-well plate readers. The excitation (blue) and detection (green) wavelengths are compatible with all common fluorimeters. QTL technical personnel can assist with configuring the settings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

**Limit of Detection comparison**



**Time Response**

