



## A Discovery Platform for Calcium Channel Blockers

*Developed at Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram*

### TECHNOLOGY AVAILABLE FOR TRANSFER

#### UNMET NEED AND OPPORTUNITY

Many diseases including brain diseases (Alzheimer's disease; stroke) and cardiovascular diseases (hypertension; arrhythmia) involve impaired functioning of calcium channel proteins. Inhibiting calcium channels using drugs is a strategy for controlling these diseases.

The Calcium Channel Inhibitor/ Blocker Market is expected to register a CAGR of 5.1 % during 2021-2026. The increasing prevalence rate of cardiovascular diseases/lifestyle disorders and changing lifestyle of people is expected to boost the calcium channel blocker market growth.

Calcium channel inhibitors are discovered by high throughput screening. The success of this process critically depends on the assay method for measuring the activity of calcium channels. For high throughput screening, simple and inexpensive techniques are desirable. Commercially available platforms for discovery of calcium channel inhibitors necessitate real-time observation of calcium ion levels in the cells.

The present technology provides a robust platform for discovery and screening of calcium channel inhibitors without the need for real time observation of calcium channel activity in the test cells.

#### TECHNOLOGY

- The technology is an end-point detection method for calcium ( $\text{Ca}^{2+}$ ) channel assays. The method uses the principle of  $\text{Ca}^{2+}$  dependent formation of a stable complex between calcium/calmodulin dependent protein kinase II (CaMKII) and a class of its ligands that interact at its T-site, as a signal for  $\text{Ca}^{2+}$  release in cells.
- The technology uses a recombinant expression system with calcium sensing protein pair, channel protein and Green Fluorescence Protein (GFP) in HEK 293 cells. The system provides a fluorescence-based readout for calcium channel activity, observed as different/changed fluorescence patterns. This approach can be used for screening of calcium channel inhibitors wherein blocking of calcium channel activation would not lead to a change in basal fluorescence pattern.
- The method does not require real time observation as the signal can be observed in fixed samples. The signal is stable for several weeks when kept under proper storage conditions.
- The technology does not need sophisticated instrumentation making it easy to perform and cost effective.
- The technology thus offers a simple, stable and economical end-point detection approach for sensing intracellular release of  $\text{Ca}^{2+}$ .

#### UNIQUE SELLING PROPOSITION

- Easy to use
- Economical
- Does not require real time observation of the calcium signal
- Test samples such as crude extracts could be evaluated for calcium channel modulating activities without any purification

#### APPLICATIONS

- Drug discovery and development of calcium channel inhibitors
- Phenotypic screening of calcium channels
- Basic biomedical scientific research

#### STAGE OF DEVELOPMENT

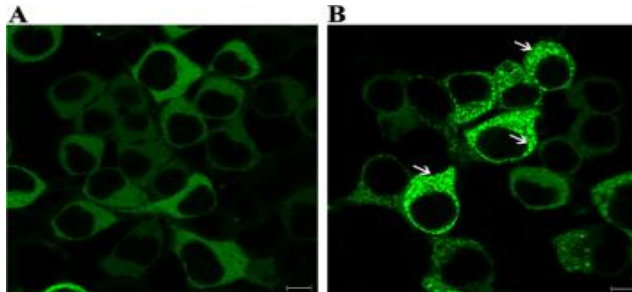


Figure: HEK-293 cells transfected with vectors carrying expression constructs, were treated with ionomycin followed by  $\text{CaCl}_2$  (B) or no  $\text{CaCl}_2$  (A). Punctate fluorescence observed as a result of calcium influx are indicated with white arrows

#### INTELLECTUAL PROPERTY

Granted patents in India, USA and European Union

#### LICENSING OPPORTUNITY

BCIL is looking for suitable partners for development and commercialization of this technology.

#### References:

1. <https://www.mordorintelligence.com/industry-reports/calcium-channel-blocker-market>
2. <https://www.frontiersin.org/articles/10.3389/fphar.2017.00286/full>
3. <https://www.liebertpub.com/doi/10.1089/adt.2009.191>

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