

Role of TRPV1 channel and P2Y1 receptor in Ca^{2+} signalling in β -cells: A study by single cell microfluorometry

Kalaiselvan Krishnan

Background

Increase in the cytosolic Ca^{2+} concentration ($[Ca^{2+}]_i$) in the pancreatic β -cells leads to insulin secretion. Tolbutamide is known to increase the $[Ca^{2+}]_i$ by closing the K_{ATP} channels leading to depolarization of the β -cells and opening of the voltage gated Ca^{2+} channels. It is unclear whether transient receptor potential (TRP) channels are involved in this process.

The mechanism by which the extracellular adenosine diphosphate ribose (ADPr) increases the $[Ca^{2+}]_i$ is currently unknown.

Objectives

- To study whether the TRP channels are involved in tolbutamide-induced $[Ca^{2+}]_i$ increase.
- To identify the surface receptor involved in the ADPr-induced Ca^{2+} increase.

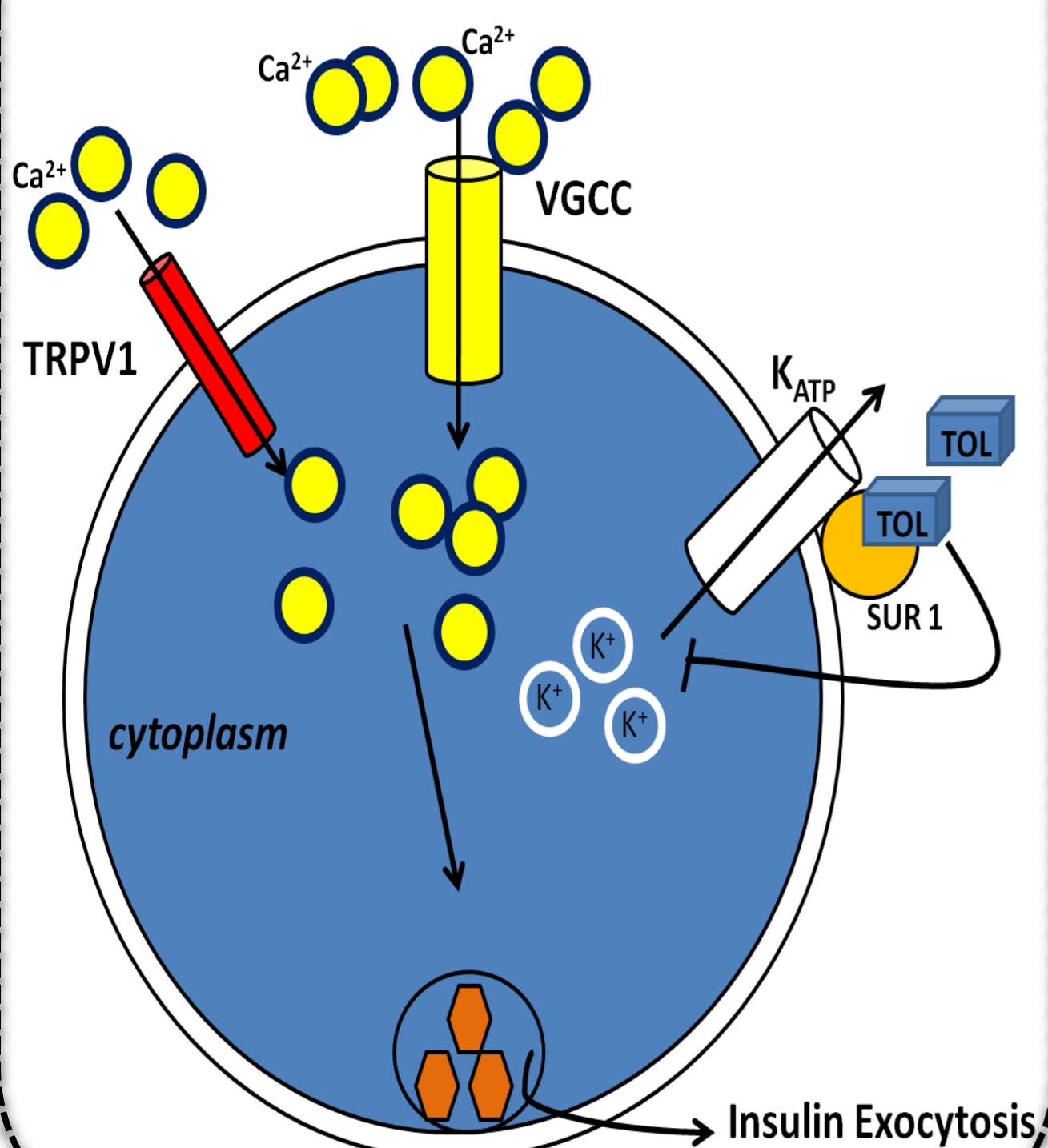
Methods

- A highly differentiated rat insulinoma cell line (S5) that was subcloned from INS-1E cells were used as model for β -cells.
- The $[Ca^{2+}]_i$ changes was measured by Fura-2-based single cell ratiometric microfluorometry.

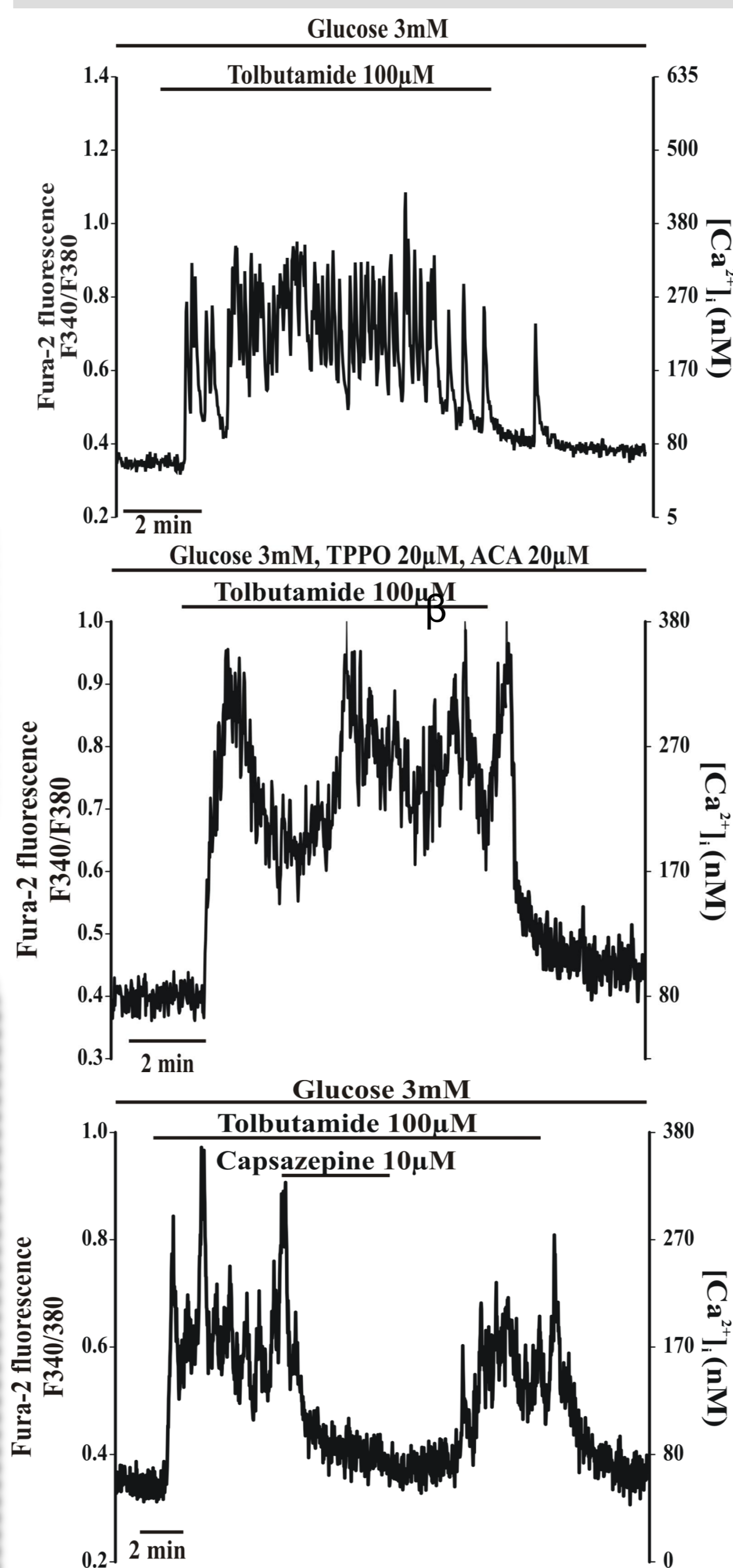
Conclusion

- Depolarization of β -cells by tolbutamide requires Ca^{2+} entry through TRPV1 channels (fig1).
- ADPr increases $[Ca^{2+}]_i$ in β -cells by activating the P2Y1 receptors.

Fig 1

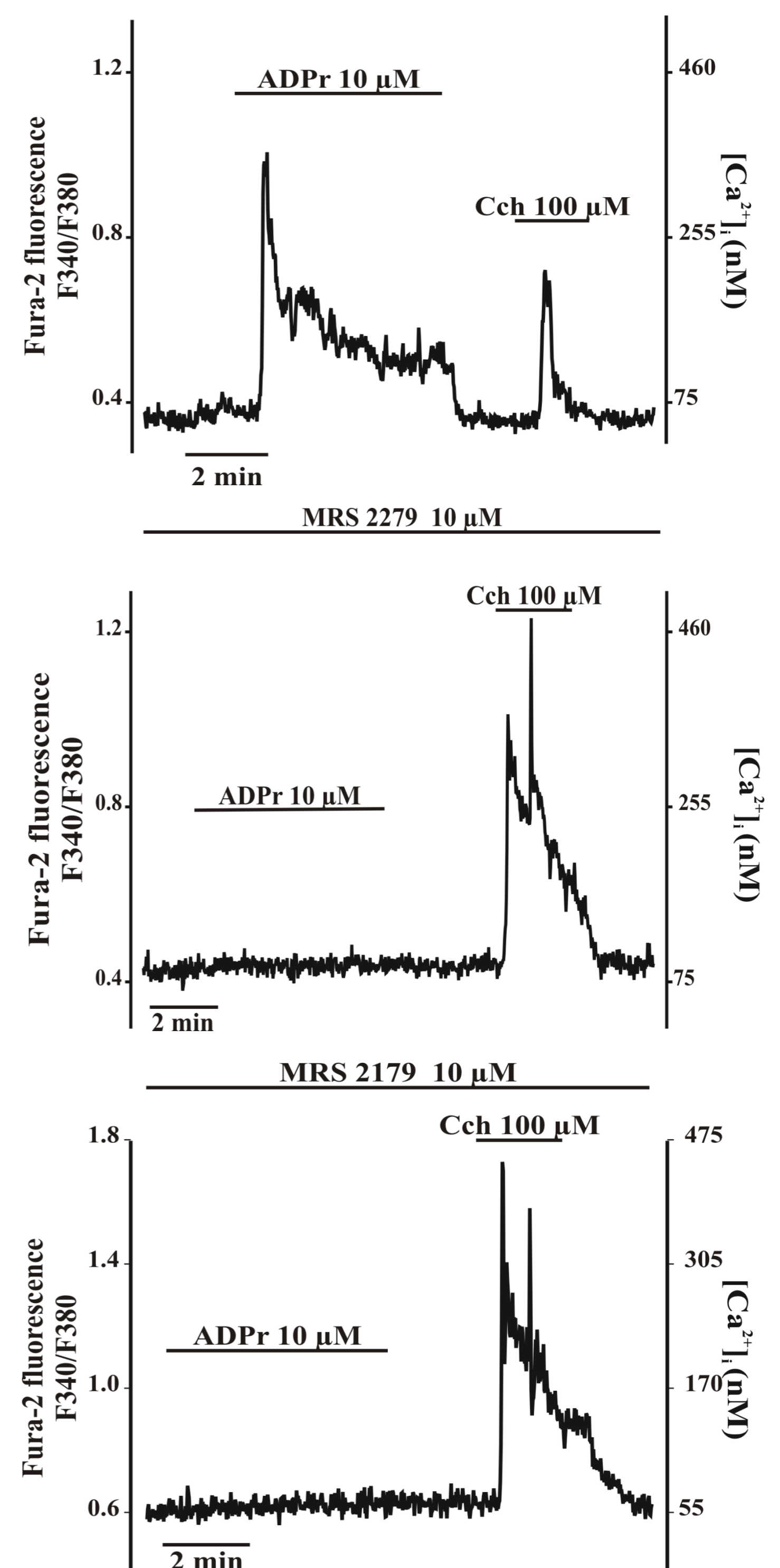


Results 1



Capsazepine, a selective inhibitor for TRPV1 channel inhibited the tolbutamide-induced $[Ca^{2+}]_i$ increase

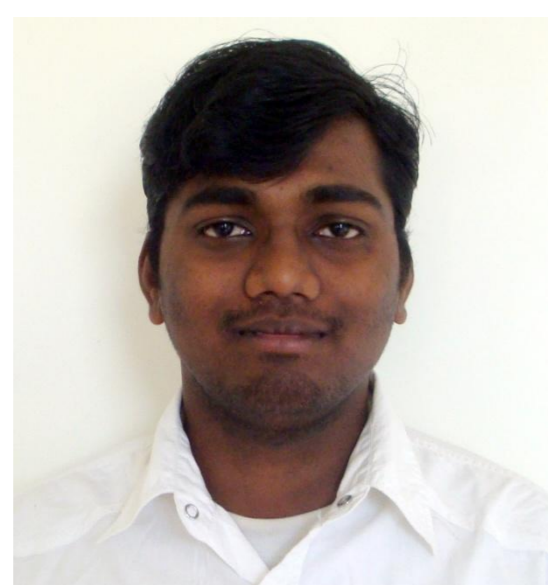
Results 2



MRS2279 and MRS2179, selective inhibitors for P2Y1 receptor inhibited the ADPr-induced $[Ca^{2+}]_i$ increase

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AUTHOR

Kalaiselvan Krishnan
Master program in Molecular genetics and physiology (2011)
Linköping University, IFM Biology, Linköping, Sweden
E-post: kalkr401@student.liu.se

SUPERVISOR

Md. Shahidul Islam
Associate professor
Karolinska Institutet, Department of Clinical Science and Education, Södersjukhuset Research Center, plan 3, 118 83 Stockholm, Sweden
E-post: shaisl@ki.se