

# NeuroD1- and Pdx1-dependent synthesis of glucokinase (Gck) protein

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# Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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### Literature references

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18,* 142. 7
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. A
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, *14*, e1005968. *オ*

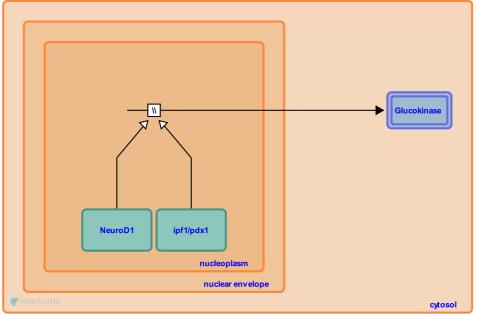
This document contains 1 reaction (see Table of Contents)

## NeuroD1- and Pdx1-dependent synthesis of glucokinase (Gck) protein 7

#### Stable identifier: R-MMU-186510

#### Type: omitted

Compartments: nucleoplasm, cytosol



NeuroD1 binds to control sequences of the mouse GK gene in vitro, and this binding is sensitive to mutagenesis in transient transfection analyses (Cissell et al. 2003; Moates et al. 2003). Moreover, NeuroD1 was shown to bind to the GK promoter in vivo by ChIP analysis and stimulate expression in pancreatic beta-cells (Moates et al. 2003).

Whether Pdx1 transactivates the glucokinase (GK) gene in vivo has been a controversial issue. Nevertheless, Pdx1 binds to control sequences of the human and mouse GK gene in vitro, and this binding is sensitive to mutagenesis in transient transfection analyses (Watada et al. 1996; Cissell et al. 2003). However, whereas Cissell et al. (2003) observed that Pdx1-specific antibodies against both the N and C termini of PDX1 selectively immunoprecipitate regulatory sequences of the GK gene, Chakrabarti et al. (2002) were unable to detect this association using a different Pdx1 antiserum. Disparity in results might be due to the different animal and cell line models used to study this regulation.

#### Literature references

- Zhao, L., Stein, R., Henderson, E., Sussel, L., Cissell, MA. (2003). Transcription factor occupancy of the insulin gene in vivo. Evidence for direct regulation by Nkx2.2. J Biol Chem, 278, 751-6.
- Chakrabarti, SK., James, JC., Mirmira, RG. (2002). Quantitative assessment of gene targeting in vitro and in vivo by the pancreatic transcription factor, Pdx1. Importance of chromatin structure in directing promoter binding. J Biol Chem, 277, 13286-93. ↗
- Stein, R., Tsai, MJ., Cissell, MA., Nanda, S., Moates, JM. (2003). BETA2 activates transcription from the upstream glucokinase gene promoter in islet beta-cells and gut endocrine cells. *Diabetes*, 52, 403-8.
- Watada, H., Yamasaki, Y., Kamada, T., Fujitani, Y., Umayahara, Y., Matsuoka, T. et al. (1996). The human glucokinase gene beta-cell-type promoter: an essential role of insulin promoter factor 1/PDX-1 in its activation in HIT-T15 cells. *Diabetes, 45,* 1478-88. *¬*

#### **Editions**

2006-12-20	Edited	Tello-Ruiz, MK.
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