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Stimulation of Human and Rat Islet beta-Cell Proliferation with Retention of Function by Nkx6.1 - Study GBCO3465

Genomics Study Specifications

Study Name	Stimulation of Human and Rat Islet beta-Cell Proliferation with Retention of Function by Nkx6.1
Contact Name	Christopher Newgard (Duke University)
Publication	http://www.ncbi.nlm.nih.gov/pubmed/18347054
My Strategies	Return to My Strategies page
Classification	Pancreas development and growth; Targets and roles of transcriptional regulators
Links	Biomaterials Graph GEO
BCBC Release Date	November 10, 2008
Public Release Date	November 10, 2008
Citation	Schisler JC, Fueger PT, Babu DA, Hohmeier HE, Tessem JS, Lu D, Becker TC, Naziruddin B, Levy M, Mirmira RG, Newgard CB. Stimulation of human and rat islet beta-cell proliferation with retention of function by the homeodomain transcription factor Nkx6.1. Mol Cell Biol. 2008. 28:3465-76

Synopsis

Study Description | Goals | Approaches | Results | Conclusions | Related Studies

The homeodomain transcription factor Nkx6.1 plays an important role in pancreatic islet beta-cell development, but its effects on adult beta-cell function, survival, and proliferation are not well understood. In the present study, we demonstrated that treatment of primary rat pancreatic islets with a cytomegalovirus promoter-driven recombinant adenovirus containing the Nkx6.1 cDNA (AdCMV-Nkx6.1) causes dramatic increases in [methyl-3H] thymidine and 5-bromo-2-deoxyuridine (BrdU) incorporation and in the number of cells per islet relative to islets treated with a control adenovirus (AdCMV-betaGAL), whereas suppression of Nkx6.1 expression reduces thymidine incorporation. Immunocytochemical studies reveal that >80% of BrdU-positive cells in AdCMV-Nkx6.1-treated islets are beta cells. Microarray, real-time PCR, and immunoblot analyses reveal that overexpression of Nkx6.1 in rat islets causes concerted upregulation of a cadre of cell cycle control genes, including those encoding cyclins A, B, and E, and several regulatory kinases. Cyclin E is upregulated earlier than the other cyclins, and adenovirus-mediated overexpression of cyclin E is shown to be sufficient to activate islet cell proliferation. Moreover, chromatin immunoprecipitation assays demonstrate direct interaction of Nkx6.1 with the cyclin A2 and B1 genes. Overexpression of Nkx6.1 in rat islets caused a clear enhancement of glucose-stimulated insulin secretion (GSIS), whereas overexpression of Nkx6.1 in human islets caused an increase in the level of [3H]thymidine incorporation that was twice the control level, along with complete retention of GSIS. We conclude that Nkx6.1 is among the very rare factors capable of

Access Status

This resource is publicly viewable.

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Primary contributor: Newgard Lab
Co-contributed by:
- Stoeckert Lab

Resource Tags

AdCMV-betaGAL, AdCMV-Nkx6.1, Ccna2, Ccnb1, Ccne1, cyclin A2, cyclin B1, cyclin E1, NK6 homeobox 1, Nkx6-1, Nkx6.1, OE.Hamster.Nkx6.1.CMV, OE.Unclassified.lacZ.CMV Ad-siNkx6.1 RNAi.Rat.Nkx6.1.HI-RNA, Operon Rat 27K Array 1

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Resource History & Actions

Approved on Nov 10, 2008
Last modified on Aug 02, 2011

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Related resources

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No matching resources

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stimulating beta-cell replication with retention or enhancement of function, properties that may be exploitable for expansion of beta-cell mass in treatment of both major forms of diabetes.

Platform types	Expression microarray, Expression
Platforms	Show platform Operon Rat 27K Array
Study Design Type	• compound_treatment_design • reference_design
Study Factors	Show study factors
Study Assays	Show study assays

Access to Study Data

This Study Data is publicly available to all users.

Gene List(s)

Use the following form(s) to refine the parameters and add the gene list to a strategy:

AdCMV-Nkx6.1 versus AdCMV-betaGAL Treated Rat Islets

|Fold Change| Greater Than: 1.5

Confidence Level: High Confidence ○ All Results ◉

For a microarray experiment a result with high confidence has a confidence level of at least 80%.

For a ChIP-chip experiment a result with high confidence has a confidence level of at least 90% and all fold changes are positive.

Reference (Denominator): AdCMV-betaGAL Islets

Find Genes

Genome Browser

There are no genome browser tracks currently available for this study.

Lists of Locations

There are no genomic location datasets currently available for this study.

Repositories

Newgard Lab

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Stock #: *Not provided*
Availability Notes: *Not provided*

Comments

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