



**QUEEN'S
UNIVERSITY
BELFAST**

Genome-wide Transcriptome Profiling of Human Trabecular Meshwork Cells treated with Dexamethasone

Senthilkumari, S., Lester, K., Lane, B., Whysall, K., Sheridan, C., Simpson, D. A., R, K. S., VR, M., & Willoughby, C. (2019). Genome-wide Transcriptome Profiling of Human Trabecular Meshwork Cells treated with Dexamethasone. *Investigative ophthalmology & visual science*, 60(9), [5669].
<https://iovs.arvojournals.org/article.aspx?articleid=2744882&resultClick=1>

Published in:

Investigative ophthalmology & visual science

Document Version:

Peer reviewed version

Queen's University Belfast - Research Portal:

[Link to publication record in Queen's University Belfast Research Portal](#)

Publisher rights

© 2019 The Authors.

This is an open access article published under a Creative Commons Attribution-NonCommercial-NoDerivs License (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits distribution and reproduction for non-commercial purposes, provided the author and source are cited.

General rights

Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.

Abstract

Purpose : The purpose of the present study was to profile genome-wide transcriptional alterations in cultured normal human trabecular meshwork (TM) cells treated with dexamethasone and also to identify the genes and gene-gene networks dysregulated by a known glaucoma stimulus.

Methods : Primary normal human TM cells (n=6) were grown to confluence and treated with 100nM dexamethasone for 16 hours. Total RNA was extracted after treatment and RNA-Seq was performed with 50 bp paired end reads (60 million reads/sample) using the Illumina NextSeq500 by Exiqon. Bioinformatics analysis used a combination of analysis components (Tuxedo, Bowtie2, Tophat, Cufflinks and Bioconductor). Gene ontology enrichment analysis was performed with a standard Fisher's test and the 'Elim' method. Ingenuity Pathway Analysis (IPA) was used for further functional analyses. Nine candidate genes were selected and validated by real time-qPCR.

Results : The read quality was high: 99.9% of reads had a Q score >30. 40-57 million reads were obtained from each sample and the average genome mapping was 82%. Differentially expressed genes (DEGs) were ranked by logFC and p values. 4793 genes were differentially expressed. Zinc Finger and BTB Domain Containing 16 (ZBTB16) and FK506 binding protein 5 (FKBP5) were the most significantly up-regulated (ZBTB16: logFC=8.3; FKBP5: logFC= 2.68) genes. Plasminogen Activator Inhibitor Type 2 (PAI) and Matrix metalloproteinase 1 (MMP-1) were the most significantly down-regulated genes (PAI: logFC=-3.59; MMP1: logFC=-1.81). IPA analysis highlighted angiogenesis, axonal guidance signalling and p38 MAPK signalling as key enriched pathways.

Conclusions : RNA-Seq is a powerful tool to investigate genome-wide alterations in gene expression in TM treated with a known glaucoma stimulus (steroid) as a hypothesis-independent approach. A number of key DEGs and pathways were identified. RNA-Seq can identify therapeutic targets for future molecular therapies to treat the TM in steroid induced glaucoma

This abstract was presented at the 2019 ARVO Annual Meeting, held in Vancouver, Canada, April 28 - May 2, 2019.