Insight Medical Publishing

ACTA PSYCHOPATHOLOGICA

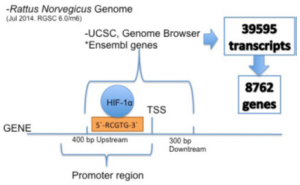
Hypoxia-inducible factor-1α (HIF-1α) binds to HIF-response elements on the promoter region of candidate genes in the genome rat under Hypoxic conditions: A bioinformatics study

Emmanuel Casanova Ortiz

University of Chile, Chile.

Abstract

Perinatal asphyxia (PA) is characterized by interruption of oxygen bioavailability at birth. Hypoxia implies HIF-1α activation, a key sentinel protein, which, upon translocation to the nucleus, binds to response elements (HREs), promoting the transcription of several genes. Potential genes activated by HIF-1α under hypoxic conditions were identified in the rat genome by extracting promoter sequences of Rattus Norvegicus from the UCSC database Genome Browser, using the latest version of rat genome. A promoter sequence of 39595 transcripts was first obtained, identifying then 8762 genes with the HIF-1α binding sequence (5`-RCGTG-3`) with the "R" software. 8762 genes were introduced to the Gene Ontology platform for performing an enrichment analysis, selecting the following processes linked to PA: Hypoxia (865 genes); Glucose metabolism (330 genes); Neurogenesis (1243 genes); Apoptosis (814 genes); Hematopoiesis (165 genes), and Regulation of gene expression (2076 genes). The 865 hypoxia associated genes were further selected and compared with experimental data by ChIP-Seq, with 772 and 98 genes, from the human and zebrafish genomes, respectively, finding that (i) 72 genes were shared by human and rat; (ii) 10 genes were shared by zebrafish and rat; (iii) 8 genes were shared by human and zebrafish, and (iv) 3 genes were shared by the three species. The 8762 genes were then analyzed by the Kyoto Encyclopedia of Genes and Genomes (KEGG) platform, selecting the HIF-1 pathway, identifying 47 genes. The 79 genes filtered for human, zebrafish and rat, were compared with the 47 genes obtained by the KEGG platform, yielding 12 genes. Finally, 12 genes were compared with 47 genes referred by the literature to be associated to PA, identifying 5 genes: Bcl2, Hif-1α, Ldha; Pdk1, and Vegfa. Analysis of sequence conservation was performed for each species, using the Ensembl Genes database, obtaining an 80% of conservative sequences for all cases.



Biography

My first approach to the area of neuroscience began in 2014 when I entered the Laboratory of Molecular and Clinical Pharmacology of the Faculty of Medicine of the University of Chile, evaluating the brain changes that occur after perinatal asphyxia, an alteration right before, during or just after delivery, which leads to the deprivation of the bioavailability of oxygen in the newborn. Previously I had worked in a genetics and genomics laboratory of the same University, which along my undergraduate profession of Medical Technologist with specialty in Morphophysiopathology and Cytodiagnosis, encouraged me to start a research focused on the genetic and genomic analysis of the brain after hypoxia. In addition to the research area, I work in the area of university management and teaching at the Universidad del Desarrollo, Santiago of Chile, and also as scientific advisor in a genetic diagnostic laboratory called Bioscan.

Publication

- Schodel J, Oikonomopoulos S, Ragoussis J, Pugh CW, Ratcliffe PJ, Mole DR. (2011). High-resolution genome-wide mapping of HIFbinding sites by ChIP-seq. Blood. 117(23): e207-17.
- Greenald D, Jeyakani J, Pelster B, Sealy I, Mathavan S, Van Eeden FJ. (2015). Genome-wide mapping of Hif-1α binding sites in zebrafish. BMC Genomics. 11; 16:923.
- Lee K.J, Lee K.Y, Lee Y.M. (2010). Downregulation of a tumor suppressor RECK by hypoxia through recruitment of HDAC1 and HIF-1alpha to reverse HRE site in the promoter. Biochim. Biophys. Acta. 1803, 608–616.
- Bergeron M, Gidday JM, Yu AY, Semenza GL, Ferriero DM, Sharp FR. (2000). Role of hypoxia-inducible factor-1 in hypoxia-induced ischemic tolerance in neonatal rat brain. Ann Neurol. 48:285–96.
- Herrera-Marschitz M, Perez-Lobos R, Lespay-Rebolledo C, Tapia- Bustos A, Casanova-Ortiz E, Morales P, Valdes JL, Bustamante D, Cassels B (2018) Targeting sentinel proteins and extrasynaptic glutamate receptors: A therapeutic strategy for preventing the effects elicited by perinatal asphyxia? Neurotoxicity Research. Volume 33, Issue 2, pp461-473.
- Neira-Pena T, Rojas-Mancilla E, Munoz-Vio V, Perez R, Gutierrez- Hernandez M, Bustamante D, Morales P, Hermoso MA, Gebicke- Haerter P, Herrera-Marschitz M. (2015). Perinatal asphyxia leads to PARP-1 overactivity, p65 translocation, IL-1β and TNF-α overexpression, and apoptotic-like cell death in mesencephalon of neonatal rats: prevention by systemic neonatal nicotinamide administration. Neurotox Res. 27(4):453-65.
- 7. Herrera-Marschitz M, Neira-Pena T, Rojas-Mancilla E, Morales P, Bustamante D, Leyton L, Gebicke-Haerter P. (2015). Short- and long-term consequences of perinatal asphyxia: looking for neuroprotective strategies. Adv Neurobiol. 10:169-98.
- Herrera-Marschitz M, Neira-Pena T, Rojas-Mancilla E, Espina- Marchant P, Esmar D, Perez R, Munoz V, Gutierrez-Hernandez M, Rivera B, Simola N, Bustamante D, Morales P, Gebicke- Haerter PJ. (2014). Perinatal asphyxia: CNS development anddeficits with delayed onset. Front Neurosci. 26;8:47..

Citation: Emmanuel Casanova Ortiz, Hypoxia-inducible factor-1α (HIF-1α) binds to HIF-response elements on the promoter region of candidate genes in the genome rat under Hypoxic conditions: A bioinformatics study, Neuroimmunology 2020, Paris, February 19-20, 2020, PP. 14