Hypoxia as a target for tissue specific gene therapy

Taiyoun Rhim, Dong Yun Lee, Minhyung Lee

PII: S0168-3659(13)00311-8
DOI: doi: 10.1016/j.jconrel.2013.05.021
Reference: COREL 6735

To appear in: *Journal of Controlled Release*

Received date: 13 February 2013
Accepted date: 24 May 2013

Please cite this article as: Taiyoun Rhim, Dong Yun Lee, Minhyung Lee, Hypoxia as a target for tissue specific gene therapy, *Journal of Controlled Release* (2013), doi: 10.1016/j.jconrel.2013.05.021

Hypoxia as a target for tissue specific gene therapy

Taiyoun Rhim†, Dong Yun Lee†, and Minhyung Lee*
Department of Bioengineering, College of Engineering, Hanyang University, Seoul 133-791, Republic of Korea

Running title: Hypoxia inducible gene therapy

†These authors contributed equally.

*Corresponding author: Minhyung Lee, Ph.D.
Department of Bioengineering, College of Engineering, Hanyang University, 17 Haengdang-dong, Seongdong-gu, Seoul 133-791, Republic of Korea
Tel: +82-2-2220-0484, Fax: +82-2-2220-1998, E-mail: minhyung@hanyang.ac.kr

Abbreviations

activating transcription factor-4 (ATF-4); aryl hydrocarbon receptor nuclear translocator (ARNT); basic helix-loop-helix (bHLH); Basso, Beattie, and Bresnahan (BBB); cellular FLICE-inhibitory protein (cFLIP); cytochrome C (cyt C); cytoglobin (Cygb); cytochrome p450 isoform 2B6 (CYP2B6); dig2 (dexamethasone-induced gene 2); DNA binding domain (DBD); erythropoietin (Epo); prolyl hydroxylases (PHDs); estrogen response element (ERE); glucagon-like peptide-1 (GLP-1); glutathione peroxidase-1 (Gpx-1); glyceraldehyde-3-phosphate dehydrogenase (GAPDH); hypoxia inducible factor-1 (HIF-1); hypoxia response element (HRE); iron responsive elements (IREs); mammalian target of rapamycin (mTOR); metallothionein (MT); microRNAs (miRNAs); oxygen dependent degradation (ODD); phosphoglycerate kinase-1 (PGK-1); reactive oxygen species (ROS); regulated in development and DNA damage responses 1 (REDD1); renal cell carcinomas (RCC); secretion signal peptide (SSP); simian virus 40 (SV40); short hairpin RNA (shRNA); *small interfering RNA (siRNA);* Src homology domain-2 containing tyrosine phosphatase-1 (SHP-1); stimulating protein-1 (SP-1); tyrosine hydroxylase (TH); unfolded protein response (UPR); untranslated region (UTR); transactivation domain (TAD); two-step transcription amplification (TSTA); vascular endothelial growth factor (VEGF); von Hippel Lindau protein (pVHL); X-linked inhibitor of apoptosis protein (XIAP)

Abstract

Hypoxia is a hallmark of various ischemic diseases such as ischemic heart disease, ischemic limb, ischemic stroke, and solid tumors. Gene therapies for these diseases have been developed with various therapeutic genes including growth factors, anti-apoptotic genes, and toxins. However, non-specific expression of these therapeutic genes may induce dangerous side effects in the normal tissues. To avoid the side effects, gene expression should be tightly regulated in an oxygen concentration dependent manner. The hypoxia inducible promoters and enhancers have been evaluated as a transcriptional regulation tool for hypoxia inducible gene therapy. The hypoxia inducible UTRs were also used in gene therapy for spinal cord injury as a translational regulation strategy. In addition to transcriptional and translational regulations, post-translational regulation strategies have been developed