

BIOGRAPHICAL SKETCH

NAME Gregg L. Semenza, M. D., Ph. D.	POSITION TITLE Professor of Pediatrics and Institute of Genetic Medicine
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EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Harvard College	A. B.	1978	Biology
University of Pennsylvania	M. D.	1984	Medicine
University of Pennsylvania	Ph. D.	1984	Genetics
Duke University Medical Center	Residency	1986	Pediatrics
Johns Hopkins University School of Medicine	Postdoc	1990	Medical Genetics

A. Positions and Honors

Professional Positions:

Assistant Professor of Pediatrics with Joint Appointment in Medicine, JHU, 1990-94
 Associate Professor of Pediatrics with Joint Appointment in Medicine, JHU, 1994-99
 Professor of Pediatrics and Institute of Genetic Medicine, Joint Appointment in Medicine, JHU, 1999-present

Awards and Other Professional Activities:

Lucille P. Markey Scholar Award in Biomedical Science, 1989-95
 Elected Member, The Society for Pediatric Research, 1991
 Elected Founding Fellow, American College of Medical Genetics, 1992
 Communicating Editor, Human Mutation, 1993-
 Established Investigator Award, American Heart Association, National Center, 1994-99
 Elected Member, American Society for Clinical Investigation, 1995
 Member, Pathobiology-2 Review Panel, US Army Breast Cancer Research Program, 1999
 Jean and Nicholas Leone Research Award, Children's Brain Tumor Foundation, 1999
 E. Mead Johnson Award for Research in Pediatrics, 2000
 Editorial Board, American Journal of Physiology: Lung Cellular Molecular Physiology, 2000-present
 Member, Hematology I NIH Study Section, 2000
 Editorial Board, Journal of Clinical Investigation, 2002-present

B. Selected Publications: (from a total of 121 since 1984)

Semenza GL and Wang GL. A nuclear factor induced by hypoxia via de novo protein synthesis binds to the human erythropoietin gene enhancer at a site required for transcriptional activation. *Mol. Cell. Biol.* 12: 5447-5454, 1992.

Wang GL and Semenza GL. General involvement of hypoxia-inducible factor 1 in transcriptional response to hypoxia. *Proc. Natl. Acad. Sci. USA* 90: 4304-4308, 1993.

Semenza GL, Roth PH, Fang H-M, and Wang GL. Transcription regulation of genes encoding glycolytic enzymes by hypoxia-inducible factor 1. *J. Biol. Chem.* 269: 23757-23763, 1994.

Wang GL and Semenza GL. Purification and characterization of hypoxia-inducible factor 1. *J. Biol. Chem* 270: 1230-1237, 1995.

Wang GL, Jiang B-H, Rue EA, and Semenza GL. Hypoxia-inducible factor 1 is a basic helix-loop-helix-PAS heterodimer regulated by cellular O₂ tension. *Proc. Natl. Acad. Sci. USA* 92: 5510-5514, 1995.

Jiang B-H, Rue E, Wang GL, Roe R, and Semenza GL. Dimerization, DNA binding, and transactivation properties of hypoxia-inducible factor 1. *J. Biol. Chem.* 271: 17771-17778, 1996.

Semenza GL, Jiang B-H, Leung SW, Passantino R, Concordet J-P, Maire P, and Giallongo A. Hypoxia response elements in the aldolase A, enolase 1, and lactate dehydrogenase A gene promoters contain essential binding sites for hypoxia-inducible factor 1. *J. Biol. Chem.* 271: 32529-32537, 1996.

Forsythe JA, Jiang B-H, Iyer NV, Agani F, Leung SW, Koos RD, and Semenza GL. Activation of vascular endothelial growth factor gene transcription by hypoxia-inducible factor 1. *Mol. Cell Biol.* 16: 4604-4613, 1996.

Jiang B-H, Semenza GL, Bauer C, and Marti HH. Hypoxia-inducible factor 1 levels vary exponentially over a physiologically relevant range of O₂ tension. *Am. J. Physiol.* 271: C1172-C1180, 1996.

Jiang, B.-H., Agani, F., Passaniti, A., and Semenza, G. L. V-SRC induces expression of hypoxia-inducible factor 1 (HIF-1) and transcription of genes encoding vascular endothelial growth factor and enolase 1: involvement of HIF-1 in tumor progression. *Cancer Res.* 57: 5328-5335, 1997.

Iyer NV, Kotch LE, Agani F, Leung SW, Laughner E, Wenger RH, Gassmann M, Gearhart JD, Lawler AM, Yu AY, and Semenza GL. Cellular and developmental control of O₂ homeostasis by hypoxia-inducible factor 1. *Genes Dev.* 12: 149-162, 1998.

Semenza GL. *Transcription Factors and Human Disease.* Oxford Univ. Press, New York, 1998.

Zhong H, Agani F, Baccala AA, Laughner E, Rioseco-Camacho N, Isaacs WB, Simons JW, and Semenza GL. Increased expression of hypoxia-inducible factor 1 in rat and human prostate cancer. *Cancer Res.* 58:5280-5284, 1998.

Yu AY, Shimoda LA, Iyer NV, Huso DL, Sun X, McWilliams R, Beaty T, Sham JSK, Wiener CM, Sylvester JT, and Semenza GL. Impaired physiological responses to chronic hypoxia in mice partially deficient for hypoxia-inducible factor 1. *J. Clin. Invest.* 102:691-696, 1999.

Zhong H, De Marzo AM, Laughner E, Lim M, Hilton DA, Zagzag D, Buechler P, Isaacs WB, Semenza GL, and Simons JW. Overexpression of hypoxia-inducible factor 1 in common human cancers and their metastases. *Cancer Res.* 59:5830-5835, 1999.

Semenza GL. Perspectives on oxygen sensing. *Cell* 98:281-284, 1999.

Kotch LE, Iyer NV, Laughner E, and Semenza GL. Defective vascularization of HIF-1-null embryos is not associated with VEGF deficiency but with mesenchymal cell death. *Dev. Biol.* 209:254-267, 1999.

Semenza GL. Regulation of mammalian O₂ homeostasis by hypoxia-inducible factor 1. *Annu. Rev. Cell Dev. Biol.* 15:551-578, 1999.

Feldser D, Agani F, Iyer NV, Pak B, Ferreira G, and Semenza GL. Reciprocal positive regulation of hypoxia-inducible factor 1 and insulin-like growth factor 2. *Cancer Res.* 59:3915-3918, 1999.

Ravi R, Mookerjee B, Bhujwala ZM, Sutter CH, Artemov D, Zeng Q, Dillehay LE, Madan A, Semenza GL, and Bedi A. Regulation of tumor angiogenesis by p53-induced degradation of hypoxia-inducible factor 1. *Genes Dev.* 14:34-44, 2000.

Zhong H, Chiles K, Feldser D, Laughner E, Hanrahan C, Georgescu M-M, Simons JW, and Semenza GL. Modulation of HIF-1 expression by the epidermal growth factor/phosphatidylinositol 3-kinase/PTEN/ AKT/ FRAP pathway in human prostate cancer cells: implications for tumor angiogenesis and therapeutics. *Cancer Res.* 60:1541-1545, 2000.

Semenza GL. HIF-1: using two hands to flip the angiogenic switch. *Cancer Metast. Rev.* 19: 59-65, 2000.

Zagzag D, Zhong H, Scalzitti JM, Laughner E, Simons JW, and Semenza GL. Expression of hypoxia-inducible factor 1 α in human brain tumors: association with angiogenesis, invasion, and progression. *Cancer* 88:2626-2618, 2000.

Sutter CH, Laughner E, and Semenza GL. HIF-1 α protein expression is controlled by oxygen-regulated ubiquitination that is disrupted by deletions and missense mutations. *Proc. Natl. Acad. Sci. USA* 97:4748-4753, 2000.

Semenza GL. HIF-1 and human disease: one highly-involved factor. *Genes Dev.* 14:1983-1991, 2000.

Aebersold DM, Burri P, Beer KT, Laissue J, Djonov V, Greiner RH, and Semenza GL. Expression of hypoxia-inducible factor-1 α : a novel predictive and prognostic parameter in the radiotherapy of oropharyngeal cancer. *Cancer Res.* 61:2911-2916, 2001.

Laughner E, Taghavi P, Chiles K, Mahon PC, and Semenza GL. HER2 (neu) signaling increases the rate of hypoxia-inducible factor 1 α (HIF-1 α) synthesis: a novel mechanism for HIF-1-mediated VEGF expression. *Mol. Cell. Biol.* 21:3995-4004, 2001.

Hirota K, and Semenza GL. Rac1 activity is required for the activation of hypoxia-inducible factor 1. *J. Biol. Chem.* 276:21166-21172, 2001.

Semenza GL. HIF-1, O₂, and the 3 PHDs: how animal cells signal hypoxia to the nucleus. *Cell* 107:1-3, 2001.

Mahon PC, Hirota K, and Semenza GL. FIH-1: a novel protein that interacts with HIF-1 α and VHL to mediate repression of HIF-1 transcriptional activity. *Genes Dev.* 15: 2675-2686, 2001.

Semenza GL. HIF-1 and tumor progression: pathophysiology and therapeutics. *Trends Mol. Med.* 8: S62-S67, 2002.

Fukuda R, Hirota K, Fan F, Jung YD, Ellis LM, and Semenza GL. IGF-1 induces HIF-1 mediated VEGF expression that is dependent on MAP kinase and PI-3-kinase signaling in colon cancer cells. *J. Biol. Chem.* 277, 38205-38211, 2002.

Semenza GL. Angiogenesis in ischemic and neoplastic disorders. *Annu. Rev. Med.* 54: 17-28, 2003.