

SELECTED PUBLICATIONS FROM NOBEL PRIZE WINNER SIR PETER J RATCLIFFE

BAKER RUSKINN

“This type of apparatus (InvivO₂) is very important for work in hypoxia, . . . it’s easy to allow inadvertent re-oxygenation to confound your experimental results. Using a controlled environment work station InvivO₂ greatly reduces that risk.”

Sir Peter J Ratcliffe

Cockman ME, Lippl K, Tian YM, Pegg HB, Figg WD Jnr, Abboud MI, Heilig R, Fischer R, Myllyharju J, Schofield CJ, Ratcliffe PJ. Lack of activity of recombinant HIF prolyl hydroxylases (PHDs) on reported non-HIF substrates. *Elife.* 2019 Sep 10;8.

Schödel J, Ratcliffe PJ. Mechanisms of hypoxia signalling: new implications for nephrology. *Nat Rev Nephrol.* 2019 Oct;15(10):641-659.

Masson N, Keeley TP, Giuntoli B, White MD, Puerta ML, Perata P, Hopkinson RJ, Flashman E, Licausi F, Ratcliffe PJ. Conserved N-terminal cysteine dioxygenases transduce responses to hypoxia in animals and plants. *Science.* 2019 Jul 5;365(6448):65-69. **Baker Ruskinn InvivO₂ 400**

Yamamoto A, Hester J, Macklin PS, Kawai K, Uchiyama M, Biggs D, Bishop T, Bull K, Cheng X, Cawthorne E, Coleman ML, Crockford TL, Davies B, Dow LE, Goldin R, Kranc K, Kudo H, Lawson H, McAuliffe J, Milward K, Scudamore CL, Soilleux E, Issa F, Ratcliffe PJ, Pugh CW. Systemic silencing of PHD2 causes reversible immune regulatory dysfunction. *J Clin Invest.* 2019 Jun 4;130:3640-3656.

Smythies JA, Sun M, Masson N, Salama R, Simpson PD, Murray E, Neumann V, Cockman ME, Choudhry H, Ratcliffe PJ, Mole DR. Inherent DNA-binding specificities of the HIF-1α and HIF-2α transcription factors in chromatin. *EMBO Rep.* 2019 Jan;20(1). **Baker Ruskinn InvivO₂ 400**

Wang Y, Zhong S, Schofield CJ, Ratcliffe PJ, Lu X. Nuclear entry and export of FIH are mediated by HIF1α and exportin1, respectively. *J Cell Sci.* 2018 Nov 19;131(22). **Baker Ruskinn InvivO₂ 400**

Markolovic S, Zhuang Q, Wilkins SE, Eaton CD, Abboud MI, Katz MJ, McNeil HE, Leśniak RK, Hall C, Struwe WB, Konietzny R, Davis S, Yang M, Ge W, Benesch JLP, Kessler BM, Ratcliffe PJ, Cockman ME, Fischer R, Wappner P, Chowdhury R, Coleman ML, Schofield CJ. The Jumonji-C oxygenase JMJD7 catalyzes (3S)-lysyl hydroxylation of TRAFAC GTPases. *Nat Chem Biol.* 2018 Jul;14(7):688-695.

Kaelin WG Jr, Ratcliffe PJ, Semenza GL. Pathways for Oxygen Regulation and Homeostasis: The 2016 Albert Lasker Basic Medical Research Award. *JAMA.* 2016 Sep 27;316(12):1252-3.

Yeh TL, Leissing TM, Abboud MI, Thinnes CC, Atasoylu O, Holt-Martyn JP, Zhang D, Tumber A, Lippl K, Lohans CT, Leung IKH, Morcrette H, Clifton IJ, Claridge TDW, Kawamura A, Flashman E, Lu X, Ratcliffe PJ, Chowdhury R, Pugh CW, Schofield CJ. Molecular and cellular mechanisms of HIF prolyl hydroxylase inhibitors in clinical trials. *Chem Sci.* 2017 Nov 1;8(11):7651-7668.

Sadiku P, Willson JA, Dickinson RS, Murphy F, Harris AJ, Lewis A, Sammut D, Mirchandani AS, Ryan E, Watts ER, Thompson AAR, Marriott HM, Dockrell DH, Taylor CT, Schneider M, Maxwell PH, Chilvers ER, Mazzone M, Moral V, Pugh CW, Ratcliffe PJ, Schofield CJ, Ghesquiere B, Carmeliet P, Whyte MK, Walmsley SR. Prolyl hydroxylase 2 inactivation enhances glycogen storage and promotes excessive neutrophilic responses. *J Clin Invest.* 2017 Sep 1;127(9):3407-3420.

Grampp S, Schmid V, Salama R, Lauer V, Kranz F, Platt JL, Smythies J, Choudhry H, Goppelt-Struebe M, Ratcliffe PJ, Mole DR, Schödel J. Multiple renal cancer susceptibility polymorphisms modulate the HIF pathway. *PLoS Genet.* 2017 Jul 17;13(7):e1006872.

Pugh CW, Ratcliffe PJ. New horizons in hypoxia signaling pathways. *Exp Cell Res.* 2017 Jul 15;356(2):116-121.

Grampp S, Platt JL, Lauer V, Salama R, Kranz F, Neumann VK, Wach S, Stöhr C, Hartmann A, Eckardt KU, Ratcliffe PJ, Mole DR, Schödel J. Genetic variation at the 8q24.21 renal cancer susceptibility locus affects HIF binding to a MYC enhancer. *Nat Commun.* 2016 Oct 24;7:13183.

Chowdhury R, Leung IK, Tian YM, Abboud MI, Ge W, Domene C, Cantrelle FX, Landrieu I, Hardy AP, Pugh CW, Ratcliffe PJ, Claridge TD, Schofield CJ. Structural basis for oxygen degradation domain selectivity of the HIF prolyl hydroxylases. *Nat Commun.* 2016 Aug 26;7:12673.

Platt JL, Salama R, Smythies J, Choudhry H, Davies JO, Hughes JR, Ratcliffe PJ, Mole DR. Capture-C reveals preformed chromatin interactions between HIF-binding sites and distant promoters. *EMBO Rep.* 2016 Oct;17(10):1410-1421. **Baker Ruskinn InvivO₂ 400**

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Chan MC, Ilott NE, Schödel J, Sims D, Tumber A, Lippl K, Mole DR, Pugh CW, Ratcliffe PJ, Ponting CP, Schofield CJ. Tuning the Transcriptional Response to Hypoxia by Inhibiting Hypoxia-inducible Factor (HIF) Prolyl and Asparaginyl Hydroxylases. *J Biol Chem.* 2016 Sep 23;291(39):20661-73.

Baker Ruskinn Invivo₂ 400

Frise MC, Cheng HY, Nickol AH, Curtis MK, Pollard KA, Roberts DJ, Ratcliffe PJ, Dorrington KL, Robbins PA. Clinical iron deficiency disturbs normal human responses to hypoxia. *J Clin Invest.* 2016 Jun 1;126(6):2139-50.

Vukovic M, Sepulveda C, Subramani C, Guitart AV, Mohr J, Allen L, Panagopoulou TI, Paris J, Lawson H, Villacreses A, Armesilla-Diaz A, Gezer D, Holyoake TL, Ratcliffe PJ, Kranc KR. Adult hematopoietic stem cells lacking Hif-1a self-renew normally. *Blood.* 2016 Jun 9;127(23):2841-6.

Chan MC, Holt-Martyn JP, Schofield CJ, Ratcliffe PJ. Pharmacological targeting of the HIF hydroxylases--A new field in medicine development. *Mol Aspects Med.* 2016 Feb-Mar;47-48:54-75.

Vukovic M, Guitart AV, Sepulveda C, Villacreses A, O'Duibhir E, Panagopoulou TI, Ivens A, Menendez-Gonzalez J, Iglesias JM, Allen L, Glykofrydis F, Subramani C, Armesilla-Diaz A, Post AE, Schaak K, Gezer D, So CW, Holyoake TL, Wood A, O'Carroll D, Ratcliffe PJ, Kranc KR. Hif-1a and Hif-2a synergize to suppress AML development but are dispensable for disease maintenance. *J Exp Med.* 2015 Dec 14;212(13):2223-34.

Hodson EJ, Nicholls LG, Turner PJ, Llyr R, Fielding JW, Douglas G, Ratnayaka I, Robbins PA, Pugh CW, Buckler KJ, Ratcliffe PJ, Bishop T. Regulation of ventilatory sensitivity and carotid body proliferation in hypoxia by the PHD2/HIF-2 pathway. *J Physiol.* 2016 Mar 1;594(5):1179-95.

Schödel J, Grampp S, Maher ER, Moch H, Ratcliffe PJ, Russo P, Mole DR. Hypoxia, Hypoxia-inducible Transcription Factors, and Renal Cancer. *Eur Urol.* 2016 Apr;69(4):646-657.

Jaakkola, P., Mole, D.R., Tian, Y.M., Wilson, M.I., Gielbert, J., Gaskell, S.J., Kriegsheim, A., Hebestreit, H.F., Mukherji, M., Schofield, C.J., et al. Targeting of HIF-alpha to the von Hippel-Lindau ubiquitylation complex by O2-regulated prolyl hydroxylation. *Science* 2001, 292, 468-472. **Baker Ruskinn Invivo₂ 400**

A.C.R.Epstein, J.M.Gleadle, L.A.McNeill, K.S.Hewitson, J.F.O'Rourke, D.R.Mole, M.Mukherji, E.Metzen, M.I.Wilson, A.Dhanda, Y.-M.Tian, N.Masson, D.L.Hamilton, P.Jaakkola, R.Barstead, J.Hodgkin, P.H.Maxwell, C.W.Pugh, C.J.Schofield, P.J.Ratcliffe. *C. elegans EGL-9 and mammalian homologs define a family of dioxygenases that regulate HIF by prolyl hydroxylation.* *Cell* 107 2001 43-54.

P.H.Maxwell, M.S.Wiesener, G.-W.Chang, S.C.Clifford, E.C.Vaux, M.E.Cockman, C.C.Wykoff, C.W.Pugh, E.R.Maher, P.J.Ratcliffe. The tumour suppressor protein VHL targets hypoxia-inducible factors for oxygen-dependent proteolysis. *Nature* 399 1999 271-275.

Masson N, Singleton RS, Sekirnik R, Trudgian DC, Ambrose LJ, Miranda MX, Tian YM, Kessler BM, Schofield CJ, Ratcliffe PJ. The FIH hydroxylase is a cellular peroxide sensor that modulates HIF transcriptional activity.. *EMBO Rep.* 13; 2012 251-7.

Schödel J, Bardella C, Sciesielski L, Brown JM, Pugh CW, Buckle V, Tomlinson IP, Ratcliffe PJ, Mole DR. Common genetic variants at the 11q13.3 renal cancer susceptibility locus influence binding of HIF to an enhancer of cyclin D1expression.. *Nature Genetics* 44 2012; 420-5.

Adam J, Hatipoglu E, O'Flaherty L, Ternette N, Sahgal N, Lockstone H, Baban D, Nye E, Stamp GW, Wolhuter K, Stevens M, Fischer R, Carmeliet P, Maxwell PH, Pugh CW, Frizzell N, Soga T, Kessler BM, El-Bahrawy M, Ratcliffe PJ, Pollard PJ. Renal cyst formation in Fh1-deficient mice is independent of the Hif/Phd pathway: roles for fumarate in KEAP1 succination and Nrf2 signaling. *Cancer Cell.* 20 2011; 524-37.

M.E.Cockman, J.D.Webb, H.B.Kramer, B.M.Kessler, P.J.Ratcliffe. Proteomics-based identification of novel factor inhibiting HIF (FIH) substrates indicates widespread asparaginyl hydroxylation of ankyrin repeat domain-containing proteins. *Molecular & Cellular Proteomics* 8, 2009; 535-546.

M.Mazzone, D.Dettori, R.L.deOliveira, S.Loges, T.Schmidt, B.Jonckx, Y.-M.Tian, A.A.Lanahan, P.Pollard, C.R.deAlmodovar, F.DeSmet, S.Vinckier, J.Aragones, K.Debackere, A.Luttun, S.Wyns, B.Jordan, A.Pisacane, B.Gallez, M.G.Lampugnani, E.Dejana, M.Simons, P.Ratcliffe, P.Maxwell, P.Carmeliet. Heterozygous deficiency of PHD2 restores tumor oxygenation and inhibits metastasis via endothelial normalization. *Cell* 136, 2009; 839-851.



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