# Patrick Maxwell FRCP FMedSci

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Date of Birth 12th March 1962

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Full Registration July 1987 No. 3129463 **GMC** Registration

#### **CURRENT POST**

In March 2002 I took up a new Chair in Renal Medicine at Imperial College London. The majority of my time is devoted to basic science research. I also have responsibility for the care of patients and clinical research in renal disease in West London, through the new West London Renal and Transplant Centre which was opened in 2005.

The principal thrust of my research is in transcriptional control of genes by oxygen. I worked on this for over ten years in Oxford with Prof Peter Ratcliffe (now FRS) before my move to set up a new laboratory at Imperial. The research program has received substantial national and international recognition and has considerable potential for translation into new therapies for patients. In 2003, with three other scientists I set up ReOx, an Oxford University spinout company, which ultimately aims to develop medicines from these discoveries.

In 2006 I was appointed Registrar of the Academy of Medical Sciences, and am involved through the Academy in aspects of national policy concerning Biomedical Science.

## PROFESSIONAL QUALIFICATIONS

BA (First class) Oxon, and subsequent MA	1983
MB BS (Distinction) London	1986
MRCP (UK)	1989
D Phil (Oxon)	1994
Accreditation and CCST in Nephrology and General (Internal) Medicine December	1996

## AWARDS, FELLOWSHIPS AND PRIZES (since qualification)

MRC Training Fellowship	1991
Senior Scholarship, Corpus Christi College, Oxford	1993
Cilag Prize, UK Renal Association	1993
Medical Research Fellowship, Corpus Christi College, Oxford	1999
Mary Evelyn Lucking prize in Medicine	1999
Martin Lockwood award (Renal Association)	2000
Fellow, Royal College of Physicians	2000
Title of Reader in Nephrology conferred by University of Oxford	2000
Goulstonian Lecturer, Royal College of Physicians	2001
Wellcome Trust Research Leave Fellowship	2001
Fellow, Academy of Medical Sciences	2005

#### **PREVIOUS POSTS**

Professor of Nephrology	Imperial College London	Renal Medicine	1/3/02 onwards
Reader in Nephrology	University of Oxford	Renal Medicine	1/9/00-28/2/02
University Lecturer	University of Oxford	Renal Medicine	1/10/96-31/8/00
Clinical Lecturer & Honorary SR	University of Oxford Medicine, Oxford	General Medicine & Renal Medicine	1/1/94 - 30/9/96
MRC Training Fellow	Institute of Molecular	Dr Ratcliffe's Group	1/10/91-31/12/94
Registrar	Lewisham Hospital	General Medicine	1/10/90-30/9/91
Registrar	Guy's Hospital	Renal Medicine	1/10/89-30/9/90
SHO	National Hospital for Nervous Diseases	Neurology	1/2/89-31/7/89
SHO	National Heart Hospital	Cardiology	1/8/88-31/1/89
SHO	St Thomas's Hospital	Intensive Care	1/2/88-31/7/88
SHO	Hammersmith Hospital	Renal Medicine	1/8/87-31/1/88
House Physician	St Thomas's Hospital	General & Renal Medicine	1/2/87-31/7/87
House Surgeon	Worthing Hospital & Southlands Hospital	Urology & General Surgery	1/8/86-31/1/87

## **UNIVERSITY (1980-1986)**

Pre-Clinical: Open scholarship to Corpus Christi College, Oxford 1980-1983 Awarded Distinction in First BM, First class honours in physiological sciences and Martin Wronker prize in Pharmacology

Clinical: Exhibition to St. Thomas's 1983-1986.

Awarded the junior medical prize (1985), and both the senior medical and surgical medals (1986). Runner up for pathology and obstetrics medals (1986). Also winner of the national MDU elective bursary competition (1985). Distinction in London MBBS Finals (Surgery, Pharmacology)

#### **RESEARCH**

For the last 15 years I have worked on cellular responses to oxygen. Key aspects have been revealing hydroxylation as a novel method of controlling protein destruction and identification of a cellular "oxygen sensor".

Fifteen years ago we set out to identify the cells in the kidney which produce erythropoietin. The rationale was (a) to identify cells which acted as oxygen sensors controlling haematocrit and (b) to gain insight into the failure of this mechanism in kidney disease. Using a transgenic approach the cells were identified as the fibroblasts (1993). Subsequent experiments demonstrated that the Ito cells of the liver also have the capacity to express erythropoietin (1994). The mice have been used to investigate new treatments for erythropoietin deficiency (2002) and to investigate the effect of renal injury on erythropoietin producing cells in the kidney (1997).

The biological importance of adapting to changes in oxygen suggested that the system might not just control erythropoietin production. We showed the underlying oxygen response system in a wide range of mammalian cells, implying that the pathway could be studied in any mammalian cell and would regulate targets besides erythropoietin (PNAS, 1993). Considerable progress has been made since; the system involves activation of a transcription factor Hypoxia Inducible Factor-1 (HIF) and controls processes ranging from angiogenesis to cellular metabolism. HIF-1 is primarily controlled through oxygen-dependent destruction of the alpha subunit. We provided the first evidence that HIF-1 is important in regulating gene expression in solid tumours (PNAS, 1997). We were also the first to show that a homologue of HIF-1 $\alpha$ , now known as HIF-2 $\alpha$ , is widely expressed and regulated through oxygen dependent proteolysis (Blood, 1998). Work on a collaborative basis showed that HIF-1α is involved in hypoxia induced apoptosis (Nature, 1998). Over the last few years we have contributed to understanding the oxygen-sensing mechanism. A key finding was that loss of the von Hippel Lindau tumour suppressor protein results in activation and stabilisation of HIF  $\alpha$  subunits (Nature, 1999). This is because VHL acts as the recognition component of an E3 ubiquitin ligase complex (J. Biol. Chem., 2000). Recently we demonstrated that an enzymatic, oxygen-dependent hydroxylation of a conserved prolyl residue in HIF-α subunits precedes recognition by VHL, providing a mechanism by which the concentration of dioxygen regulates HIF activation (Science, 2001). Subsequently we have identified the enzymes (Cell, 2001), and also solved the structure of the HIF:VHL complex (Nature, 2002). Recently collaborative work showed that congenital polycythaemia can be caused by homozygosity for a subtle defect in VHL (Nature Genetics, 2002), or a heterozygous mutation in one of the HIF hydroxylases (PNAS 2006).

My current program is focused on the link between VHL loss and kidney cancer, and the therapeutic potential of potentiating HIF activation by inhibiting the hydroxylase enzymes.

#### **PUBLICATIONS**

Those considered to be of particular importance are marked in the margin.

## **Articles**

- 1. Hill P, Shukla D, Tran MG, Aragones J, Cook HT, Carmeliet P, Maxwell PH. Inhibition of hypoxia inducible factor hydroxylases protects against renal ischemia-reperfusion injury. J Am Soc Nephrol. 2008. 19:39-46
- 2. Aragonés J, Schneider M, Van Geyte K, Fraisl P, Dresselaers T, Mazzone M, Dirkx R, Zacchigna S, Lemieux H, Jeoung NH, Lambrechts D, Bishop T, Lafuste P, Diez-Juan A, Harten SK, Van Noten P, De Bock K, Willam C, Tjwa M, Grosfeld A, Navet R, Moons L, Vandendriessche T, Deroose C, Wijeyekoon B, Nuyts J, Jordan B, Silasi-Mansat R, Lupu F, Dewerchin M, Pugh C, Salmon P, Mortelmans L, Gallez B, Gorus F, Buyse J, Sluse F, Harris RA, Gnaiger E, Hespel P, Van Hecke P, Schuit F, Van Veldhoven P, Ratcliffe P, Baes M, Maxwell P, Carmeliet P. Deficiency or inhibition of oxygen sensor Phd1 induces hypoxia tolerance by reprogramming basal metabolism. Nature Genetics. 2008 Jan 6; [Epub]
- 3. Angelillo-Scherrer A, Burnier L, Lambrechts D, Fish RJ, Tjwa M, Plaisance S, Sugamele R, DeMol M, Martinez-Soria E, Maxwell P, Lemke G, Goff SP, Matsushima GK, Earp HS, Chanson M, Collen D, Izui S, Schapira M, Conway EM & Carmeliet P. Role of gas6 in erythropoiesis and anemia. 2008 J Clin Invest (in press)
- 4. Smith TG, Brooks JT, Balanos GM, Lappin TR, Layton DM, Leedham DL, Liu C, Maxwell PH, McMullin MF, McNamara CJ, Percy MJ, Pugh CW, Ratcliffe PJ, Talbot NP, Treacy M, Robbins PA. Mutation of the von Hippel-Lindau gene alters human cardiopulmonary physiology. Adv Exp Med Biol. 2008;605:51-6.
- 5. Pepper RJ, Gale DP, Wajed J, Bommayya G, Ashby D, McLean A, Laffan M, Maxwell PH. Inadvertent postdialysis anticoagulation due to heparin line locks. Hemodial Int. 2007;11:430-4.
- 6. Rajatapiti P, van der Horst I, de Rooij J, Tran M, Maxwell P, Tibboel D, Rottier R, De Krijger R. Expression of hypoxia-inducible factors in normal human lung development. Pediatr Dev Pathol. 2007 Jul 2;:1 [Epub ahead of print]
- 7. Wiesener MS, Munchenhagen P, Glaser M, Sobottka BA, Knaup KX, Jozefowski K, Jurgensen JS, Roigas J, Warnecke C, Grone HJ, Maxwell PH, Willam C, Eckardt KU. Erythropoietin gene expression in renal carcinoma is considerably more frequent than paraneoplastic polycythemia. Int J Cancer. 2007;121:2434-42
- 8. Pollard PJ, Spencer-Dene B, Shukla D, Howarth K, Nye E, El-Bahrawy M, Deheragoda M, Joannou M, McDonald S, Martin A, Igarashi P, Varsani-Brown S, Rosewell I, Poulsom R, Maxwell P, Stamp GW, Tomlinson IP. Targeted inactivation of th1 causes proliferative renal cyst development and activation of the hypoxia pathway. Cancer Cell. 2007;11:311-9.
- 9. Zwerts F, Lupu F, De Vriese A, Pollefeyt S, Moons L, Altura R, Jiang Y, Maxwell PH, Hill P, Oh H, Rieker C, Collen D, Conway SJ, Conway EM. Lack of endothelial cell survivin causes embryonic defects in angiogenesis, cardiogenesis, and neural tube closure. Blood. ;109:4742-52.
- 10. Kiriakidis S, Esteban M A, Maxwell P H. Genetic insights into the hypoxia-inducible factor (HIF) pathway. Elsevier, Advances in Enzyme Regulation. 2006;47:288-306
- 11. Boutet A, De Frutos CA, Maxwell PH, Mayol MJ, Romero J, Nieto MA. Snail activation disrupts tissue homeostasis and induces fibrosis in the adult kidney. EMBO J. 2006;25:5603-13.
- 12. Vortmeyer A, Tran M, Zeng W, Glasker S, Riley C, Tsokos M, Ikejiri B, Merrill M, Raffeld M, Zhuang Z, Lonser R, Maxwell P, Oldfield E. Evolution of VHL tumourigenesis in nerve root tissue. J Pathol. 2006:210:374-82.
- 13. Kinderlerer AR, Steinberg R, Johns M, Harten S, Lidington EA, Haskard DO, Maxwell P, Mason JC. Statin-Induced Expression of CD59 on Vascular Endothelium in Hypoxia. A Potential Mechanism for the Anti-inflammatory Actions of Statins in Rheumatoid Arthritis. Arthritis Res Ther. 2006;8:R130.
- 14. Glasker S, Tran M, Shively S, Ikejiri B, Lonser R, Maxwell P, Zhuang Z, Oldfield E, Vortmeyer A. Epididymal cystadenomas and epithelial tumourlets: effects of VHL deficiency on the human epididymis. J Pathol. 2006;210:32-41.

- 15. Walmsley SR, Cowburn AS, Clatworthy MR, Morrell NW, Roper EC, Singleton V, Maxwell P, Whyte MK, Chilvers ER. Neutrophils from patients with heterozygous germline mutations in the von Hippel Lindau protein (VHL) display delayed apoptosis and enhanced bacterial phagocytosis. Blood. 2006;108:3176-8.
- 16. Willam C, Maxwell PH, Nichols L, Lygate C, Tian YM, Bernhardt W, Wiesener M, Ratcliffe PJ, Eckardt KU, Pugh CW. HIF prolyl hydroxylases in the rat; organ distribution and changes in expression following hypoxia and coronary artery ligation. J Mol Cell Cardiol. 2006;41:68-77.
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- 19. Esteban MA, Tran MG, Harten SK, Hill P, Castellanos MC, Chandra A, Raval R, O'Brien TS, Maxwell PH. Regulation of E-cadherin expression by VHL and hypoxia-inducible factor. Cancer Res. 2006;66:3567-75.
- 20. Chen S, Zhou Y, Li X, Huang S, Huang W, Zhou C, Maxwell P, Wang Y. Genetic and structural analyses suggest that a novel SPG3A mutation causes severe henotypes of hereditary spastic paraplegia. Chinese Science Bulletin 2006;51:2038-2040.
- 21. Du Roure C, Takacs K, Maxwell PH, Roberts I, Dazzi F, Cannella L, Merkenschlager M, Fisher AG. Correction of severe anaemia using immuno-regulated gene therapy is achieved by restoring the early erythroblast compartment Br J Haematol. 2006;132:608-14.
- 22. Wang S, Voisin MB, Larbi KY, Dangerfield J, Scheiermann C, Tran M, Maxwell PH, Sorokin L, Nourshargh S. Venular basement membranes contain specific matrix protein low expression regions that act as exit points for emigrating neutrophils. J Exp Med. 2006;203:1519-32
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- of HIF-1alpha and -2alpha in cardiomyocytes and stromal cells of ischemic myocardium. FASEB J. 2004;18:1415-7.
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#### **INVITED EXTERNAL SEMINARS ETC OVER LAST 4 YEARS**

January 2008: von Hippel Lindau disease. Invited speaker/lecture, Advanced Nephrology Course Part 2, Royal College of Physicians, London, UK

November 2007: New treatments for APKD and everything you wanted to know about other cystic kidney diseases. Invited lecture/speaker. Nephrology Network 2007. Hertfordshire, UK.

September 2007: The implication of HIF in the kidney. Invited lecture/speaker. 9e Réunion Commune, Societe de Nephrologie, Societe Francophone de Dialyse. Lyon, France.

July 2007: Frontiers in Renal Science – Genetics, Inflammation and Repair. Chair. European Renal Association, European Dialysis and Transplant Association (ERA-EDTA).CME Course. Oxford, UK. June 2007: Prolyl hydroxylases and regulation of HIF-1 activity. Invited speaker. 6<sup>th</sup> Parnas Conference. Krakow, Poland.

May 2007: Laboratory Science Session and Moderator, Poster Session. Chair. Renal Association Annual Conference 2007. Brighton, UK.

May 2007: Hypoxia-inducible factor 1 and oxygen sensing. Invited speaker. Institute for Cancer Research. Sutton, UK.

April 2007: Invited Seminar. Cancer Centre, The Massachusetts General Hospital. Boston, USA.

February 2007: Hypoxia-inducible factor VHL & oxygen sensing. Invited speaker. Asan Medical Centre. Seoul Korea

February 2007: Deregulation of HIF in VHL and other diseases. Invited lecture/speaker. University of Maastricht.

January 2007: Hypoxia inducible factor-1 & oxygen sensing. Invited lecture/speaker. London Metabolic Discussion Group. London, UK.

November 2006: Oxygen-sensing and the kidney. Invited seminar. Renal Department. Queen Elizabeth Hospital, Birmingham, UK.

November 2006: Channels and Transporters group. Invited seminar. University of Manchester, UK.

October 2006: The 7<sup>th</sup> International Symposium on VHL and hereditary kidney cancers. VHL Family Alliance. Ontario, Canada. Member of International Scientific Committee and plenary speaker.

September 2006: The VHL tumour suppressor gene. Invited lecture. British Society of Human Genetics. Annual Meeting. York.

September 2006: The VHL-HIF pathway. The Special Symposium Lecture, 47<sup>th</sup> Advances in Enzyme Regulation Meeting. Bologna, Italy.

August 2006: The role of HIF and VHL in cancer. Invited lecture. First International Congress of Respiratory Biology, Bad Honnef, Germany.

May 2006: The HIF system as a therapeutic target. Invited lecture. 20<sup>th</sup> meeting of the London Clinical Pharmacology Group.

May 2006. The case against haemoglobin target individualisation. Global Expert Meeting – Anemia Management, Hamburg. Invited debate with Dr I. MacDougall.

May 2006: Hypoxia Inducible Factor. Invited seminar. Beth Israel Deaconess Medical Centre, Boston.

April 2006: HIF-1 and Oxygen Sensing. Invited seminar. Institute of Reproductive and Developmental Biology. Hammersmith London

April 2006: HIF-1 – a missing link between metabolism and cancer. Invited lecture. Actualities Nephrologiques. Necker seminar (retirement of Prof J-P Grunfeld). Paris.

March 2006: The impact of HIF and CA9 in tumorigenesis. Invited lecture. Federation of Experimental Physiology Societies meeting. Munich.

March 2006: HIF-1 and Oxygen Sensing. Invited seminar. Centre for Inflammation Research, Edinburgh.

February 2006: HIF-1 as a therapeutic target. Invited lecture. Frontiers in Rheumatology, London.

January 2006: Regulation of E-cadherin by VHL and HIF. Invited lecture. Keystone conference – Hypoxia and development, physiology and disease. Breckenridge, Colorado.

November 2005: Hypoxia-inducible factor. Invited Speaker. 19eme seminaire fondamental de Nephrologie. Paris.

November 2005: "Targeted Gene Deletion in the Thick Ascending Limb of the Mouse Kidney". And "the von Hippel Lindau Protein Regulates E-Cadherin in Renal Epithelium Via Hypoxia Inducible Factor." Oral Presentations. American Society of Nephrology Renal Week 2005, Philadelphia, USA.

June 2005: Erythropoietin: biology and clinical applications. Invited Speaker. Advances in Haematology meeting.

June 2005: "Erythropoietin: biology and clinical applications". Invited lecture. 37<sup>th</sup> Annual Advances in Haematology seminar, Hammersmith Hospital, London, UK.

May 2005: "HIF-1 in cancer – a target for therapy?". Invited lecture. Department of Endocrinology and Metabolic Medicine seminar, St Mary's Hospital, London.

April 2005: "The Histology of VHL Specific Renal Cell Carcinoma". Invited lecture. The Nordic Workshop on Von Hippel-Lindau disease, Copenhagen.

April 2005: "HIF- 1 and Molecular Regulation of Oxygen Homeostasis". Invited lecture. The National Kidney Research Fund Fellows' Day. Renal Association & British Transplantation Society Joint Congress, Belfast.

April 2005: "HIF-1 and Molecular Regulation of Oxygen Homeostasis". Invited lecture. International Congress of Physiological Sciences (IUPS 2005). San Diego, California.

March 2005: "Can we manipulate cellular oxygen responses for therapeutic benefit?" Invited lecture. Erlangen University, Nuremburg, Germany.

March 2005: "The Elixir of Life". Invited lecture. The 246<sup>th</sup> Meeting of the Circle of Willis Queens College, Oxford.

December 2004: "How cells sense and respond to changes in oxygen". Invited lecture. GROW Science Day, Research Institute Growth and Development, Maastricht, the Netherlands.

November 2004: "The role of hypoxia in the progression of diabetic complications". Invited lecture. ACORD investigators meeting, Amsterdam.

November 2004: "HIF-1 and mechanisms of oxygen sensing". Invited lecture. University of Utrecht, the Netherlands.

October 2004: "Regulation of oxygen sensing and erythropoietin production". Invited lecture. Disorders of Erythropoiesis and Iron Metabolism Conference, European School of Haematology (ESH), Genoa, Italy.

September 2004: "Genetics of Renal Disease: where are we now and where are we going to?". Organizer and invited lecture. Renal Association Autumn Meeting, Barbican, UK.

July 2004: "Hypoxia sensing and implications in nephrology". Invited lecture. Nephrology summer training school, Frankfurt, Germany.

June 2004: "Role of VHL in regulating HIF". 9<sup>th</sup> International workshop on multiple endocrine neoplasia meeting. Invited lecture. National Institute of Health, the NIH/FAES CME Committee, Bethesda, Maryland.

June 2004: "HIF-1 and oxygen sensing". Invited lecture. Emory University School of Medicine Elkin Lecture Series, Winship Cancer Institute, Atlanta, Washington DC.

May 2004: "Hypoxia Inducible Factors and Regulation of Hypoxic Responses". Invited lecture/chair. 6th International symposium on von Hippel-Lindau Disease, Kochi, Japan.

May 2004: "Mechanisms of oxygen sensing". Invited lecture, European Renal Association-European Dialysis and Transplant Association, Lisbon, Portugal.

April 2004: "Upstream of erythropietin. How does the kidney sense haematocrit?". Invited lecture. Société Québecoise de Néphrologie -Satellite Conference, Quebec, Canada.

March 2004: "HIF-1 and Cancer". Invited lecture. Aventis laboratories, Paris.

November 2003:"HIF-1, oxygen sensing and angiogenesis". Invited lecture. LRF/UKMF Workshop on Angiogenesis, Royal Society of Medicine, London, UK.

October 2003: "Identification of renal impairment and prevention of progression". Invited lecture. The Royal College of Physicians, London, UK.

October 2003: "A genetic approach to IgA nephropathy". Invited lecture. West London Renal Research Forum, Imperial College London, UK.

October 2003: "Erythropoietin, polycythaemia and oxygen sensing". Invited lecture. Queen's University, Belfast.

September 2003: "Intracellular proteolysis and oxygen sensing". Invited lecture. 13th International Symposium on Atherosclerosis, Kyoto, Japan.

September 2003: "2-oxoglutarate dependent dioxygenases regulating HIF-1". Invited lecture. 43rd Advances in Enzyme Regulation meeting, Indianapolis, USA.

June 2003: "Carbonic anhydrase and tumour hypoxia. Invited lecture. 6<sup>th</sup> International Conference on Carbonic Anhydrases, Bratislava.

June 2003: "Hypoxia induced genes". Invited lecture. Satellite symposium to the ISN-ERA/EDTA-World Congress of Nephrology, Bavaria, Germany.

May 2003: World Congress on Iron Metabolism, Washington DC. Session chair and invited speaker.

May 2003: Invited speaker. Academic Day for Mark Walport's farewell seminar, Imperial College London, UK.

May 2003: "Basic and clinical science of erythropoietin". Invited lecture. Canadian Society of Nephrology, Newfoundland, Canada.

May 2003: "From the lab to the bedside and back". Invited lecture. Corpus Christi College Medical Society, Oxford, UK.

April 2003: "Oxygen sensing and HIF-1". Invited lecture. Rudbeck Seminar series on "hypoxia", Uppsala.

March 2003: "Hormones and the Kidney". Invited lecture. Joint meeting between Endocrine and Renal Sections, Royal Society of Medicine, London, UK.

February 2003: "Regulation of HIF-1". Invited lecture. Invited speaker. Oxygen homeostasis and hypoxia meeting, National Cancer Institute, Washington DC.

#### **GRANTS**

# **Current funding:**

The Olive Adams Bequest (HHTRC). Developing a comprehensive Renal Biobank. £240,183. 2007

**BRC Research Grant.** Project Grant. Collection of DNA samples from patients with renal disease and controls. £45,000. 2007

**BUF Research Grant.** Clinical training fellowship for R. Barod. The Role of hypoxia inducible factor (HIF) system in renal cell carcinoma. £35,000. 2007-2008

**Cancer Research UK.** Project grant. "Role of the VHL/HIF pathway in epithelial to mesenchymal transitions £170,000. Commences; 1<sup>st</sup> December 2006 for 3 years

Hammersmith Hospital Trustees Research Committee. Does variation in selctin, megsin and IGHMBP2 genes contribute to IgA nephropathy in the UK? £9000. Nov 2005 - 2006

**Medical Research Council.** Training fellowship for Dr D. Gale. Familial ertyhrocytosis and altered oxygen sensing a genetic and clinical investigation. £180,000. Commencing Nov 2006 for 3 years.

**BBSRC Integrative Mammalian Biology Award.** 2006. £3.5m. Co-applicant. Capacity building award in in vivo research. Will fund an MRes course, PhD studentships and tenure-track lecturer posts.

The Royal College of Surgeons of England/National Kidney Research Fund. Clinical training fellowship for R. Barod. The role of the hypoxia inducible factor system in kidney cancer. £120,000. Nov 2005 over 2 years.

**British Heart Foundation:** PhD Studentship grant for Mr Modassar Khan. Would inhibitors of the asparaginyl hydroxylase FIH (Factor inhibiting HIF) be useful in ischaemic disease? April 2005. £80,170 over 3 years.

**Cancer Research UK:** Project grant. Role of the von Hippel Lindau tumour suppressor in regulating intercellular adhesion. Sept 2004. £180,000 over 3 years.

**The European Commission Framework 6:** Integrated project. "Targeting newly discovered oxygensensing cascades for novel cancer treatments: biology, equipment, drug candidates". February 2004. Share of grant Euro 452,780 over five years.

**Guy's & St Thomas NHS Trust Urology Fund:** "How does the VHL tumour suppressor act as a gatekeeper in renal epithelium". February 2006. £10,000 over two years.

**British Heart Foundation**: Programme grant. Evaluation of HIF prolyl hydroxylases as a therapeutic target in myocardial ischaemia. May 2003. £809,660 over five years.

#### **Previous Key Grants:**

**Cancer Research UK:** Project grant. "Manipulation of the VHL-HIF axis in the kidney". £255,000. June 2002 – August 2005.

**Medical Research Council**: Clinical Research Training Fellowship for Miss M. Tran. "How does the VHL tumour suppressor protein act as gatekeeper in renal epithelium?". April 2003. £148,000 over 3 years.

**Wellcome Trust**: Clinical Training Fellowship for Dr P. Hill. "The biological role of HIF prolyl hydroxylases". November 2003. £183,747 over three years.

**Wellcome Trust**: Travelling fellowship for Dr Miguel Esteban Barragan. "Characterization of enzyme-substrate interactions underlying the regulation of Hypoxia-Inducible Factor by oxygen sensitive hydroxylases". January 2004. £91,638 over two years.

**Wellcome Trust:** Research Leave Fellowship. August 2001 over 5 years. £353,188. Resigned 1<sup>st</sup> March 2002.

**Wellcome Trust.** Program grant (co-applicant with Professor P. Ratcliffe and Professor C.Pugh) to study regulation of gene expression by oxygen. £1.5m. June 2000 – May 2005.

**Science Research Investment Fund** Centre for Cellular and Molecular Physiology (£3.86m; coapplicants R.Thakkar, R.Cornall, C.Pugh, P.Ratcliffe).

#### **PATENTS**

I am co-inventor on a patent concerning the HIF-pVHL interaction as a screening system for molecules able to potentiate or interfere with the hypoxic response (GB patent 99/11047). I am also co-inventor on patents concerning HIF Hydroxylases (PCT/GB02/01381) for world IPO patent organization W002/074981 published 26/09/02, and HIF Hydroxylase Inhibitors (PCT/GB03/01239) for World IPO patent organization WO 03/080566 published 02/10/2003. I am also co-inventor on patents concerning Assays, Methods and means relating to Hypoxia inducible factor (HIF) Hydroxylase for European Patent (GB patent 0201381). I am also co-inventor on a patent concerning Ischaemia Therapeutics project (PCT/GB00/01826) for ISIS University of Oxford Innovation patent no. US6,787,326 B1 published 07/09/2004.

# **CONSULTANCY**

I have undertaken consultancy work for ReOx, Bayer, Oxford Biomedica, Bioenvision, Powderject and Roche.

# ADMINISTRATIVE and EDUCATIONAL RESPONSIBILITIES, PROFESSIONAL SOCIETIES etc IMPERIAL COLLEGE

**Programme Director**, Integrated Academic Training in Nephrology. Academic Clinical Fellow and Clinical Lecturer posts (awarded all posts requested – 10 ACF's over 5 years, 3 CL posts over 5 years 2006-2011)

Renal Co-theme leader, Imperial Biomedical Research Centre. 2006 - .

Faculty committees: Postgraduate medical training committee, RAE committee

**Divisional/campus committees:** Central Biomedical Services (HH) Committee, Campus Strategy Committee, West London Renal and Transplant Research Board, Division of Medicine Executive Committee, Division of Medicine Research Committee (Chair), Hammersmith Hospital Trustee's Research Committee (HHTRC).

Teaching: I have regular commitments teaching on the following courses

- Nephrology Update Course (co-organiser)
- Renal Biopsy Course (co-organiser)
- MSc in Molecular Medicine
- BSc Immunity and Infection
- BSc Vascular Biology
- Integrated body function and dysfunction course (2<sup>nd</sup> year MBBS).

#### **PhD Students Supervised To Completion:**

PhD: Matthew Cockman, University of Oxford (supervisor)

PhD: Maxine Tran, Imperial College, University of London (supervisor)

PhD: Jerome Brooks, University of Oxford (co-supervisor)

#### **Student Prizes:**

Maxine Tran: RSM Clinicopathology (Urology) prize (awarded 2006)

Sarah Harten: Graduate School of Life Science and Medicine Poster prize (2006)

Ravi Barod: RSM Urology Section Short Papers Prize (2006) and Alcock's Society - Johnson Prize for Best Surgical Presentation (2007)

Ta Lim (current co-supervised PhD student) Royal College of Anaesthetists' President's Prize for best poster

Ayesha Iriza-Ali, Imperial College, Hammersmith Hospital (MSc supervisor) [awarded Distinction]

**Academic Mentor to Senior Lecturers:** Dr Matthew Pickering, Rheumatology/Medicine; Dr Duncan Bassett, Investigative Sciences/Endocrinology. Dr Paul Evans, NHLI /Cardiovascular Biology, Dr Paul Elkington NIHR Clinician Scientist

#### **EXTERNAL**

#### Site Visits:

Science Foundation Ireland. November 2005: Dublin, Science Foundation Ireland – site visit for Cormac Taylor, SFI investigator.

Cancer Research UK. January 2006: Glasgow, The Beatson Institute. Mid term review for Eyal Gottlieb. St Vincent's University Hospital, Dublin. July 2006: International Review Panel of Research

#### Theses examined:

PhD: Koen Brusselmans University of Leuven

D.Phil: Kathryn Elliott University of Oxford

PhD: Dagan Jenkins, London University

PhD: Gareth Jones, London University

PhD: Chong-Hai Gan, London University

PhD: Jun Yang, The Institute of Cancer Research: Royal Cancer Hospital, Surrey

#### Peer review:

I referee manuscripts for Nature Medicine, Nature Cell Biology, Experimental Nephrology, Kidney International, Blood, the British Journal of Haematology, Oncogene, Cancer Research, the American Journal of Pathology, EMBO reports and Science. I have refereed grant applications for the Wellcome Trust, Glaxo Smith Kline, Israel Science Foundation, the Yorkshire Cancer Research Campaign, the MRC, The Royal Society of New Zealand, the National Kidney Research Fund and Cancer Research LIK

#### National and International activities:

European Commission Research Directorate-General: ERC Starting Grants Evaluation Panel. "Medical and health science research – LS6". September 2007

The Wellcome Trust Clinical Fellowship Committee 2007 onwards

National Institute of Health Research Advisory Board – 2007 onwards

Board member, UK Clinical Research Collaboration, 2007 onwards

Member of the MMC England Programme Board. June 2007 onwards

Wellcome Trust Knock Mouse Resource Committee. London. February 2007

Member, MRC College of Experts - affiliated to the Molecular & Cellular Medicine Board (MCMB). June 2006 onwards

Registrar, Academy of Medical Sciences. 2006 onwards. Chair RITA working group.

The Wellcome Trust Physiological Sciences Funding Committee. 2004 to 2007

Scientific Advisory Board, Roche Foundation for Anaemia Research (RoFAR) 2003 onwards

#### Professional societies:

I have been a member of the Renal Association since 1990, and have given oral presentations at many meetings. I was a member of their Working Party on Training, Education, Research in July 2004. I am also a member of the European Renal Association, the International IgA network and the Association of Physicians. I was elected Fellow of the Royal College of Physicians in May 2000 and Elected Fellow of the Academy of Medical Sciences in 2005. Appointed as Registrar, Academy of Medical Sciences, 2006.

Member of the International Scientific Committee for the VHL Family Alliance's meetings 2004-2008. I am a member of the NKRF External Referee Panel and of the UK Renal Association and European Renal Association-EDTA paper selection committees for their annual meetings. I have judged the MRS/AMS Young investigators meeting (2003, 2006)