CURRICULUM VITAE - DR ROBERT WILLIAM GRISTWOOD

Date of birth:	28. 09. 1952
Nationality:	British
Address	Sebel House, 3 Owls Close, Whittlesford, Cambridge CB22 4PL UK.
Educated:	Nobel Grammar School Stevenage, U.K. (1964-1970) North Hertfordshire College, U.K. (1970-1972) North East London Polytechnic, U.K. (1972-1976) BSc Smith Kline in collaboration with University of Oxford, U.K. (1978-1982) PhD
Qualifications	BSc (Applied Biology), PhD (Pharmacology)
Society Membership (Present or past)	British Pharmacological Society Biochemical Society British Toxicology Society Society of Medicines Research Sociedad Espanola de Farmacologia
Editorial functions	Editor of British Journal of Pharmacology 1992 - 1997 Editor of Journal of Cardiovascular Pharmacology 1987 - 1995 Editor of Expert Opinion on Investigational Drugs 1992 – 2006 Editor of Current Opinion in Anti-inflammatory and Immunomodulatory Investigational Drugs 1997-2000

Employment

1974-1975. Pharmacological research in the department of Medicinal Biology, Pfizer Central Research, Sandwich, Kent, U. K. Spent 1 year on research which was in support of the PDE (phosphodiesterase) inhibitor cardiac stimulant programme and the development of the selective PDE inhibitor buquineran.

1976-1988. Cardiovascular/ respiratory pharmacological / biochemical research within Pharmacology department, Smith Kline Research Ltd. Welwyn, U.K. Final position was Associate Director of Pharmacology, Head of cardiovascular, respiratory and electrophysiology groups. Direct reporting staff, 3 PhDs, 6 graduates, 1 undergraduate and 1 research fellow. Carried out a variety of cardiovascular, respiratory and electrophysiological

investigations, a number of which have been reported in the literature (see references). Initial work (including PhD thesis) was concerned with histamine receptors and possible additional clinical utilities of the H_2 antagonist cimetidine. Was later leader of a major research programme concerned with the identification of novel agents for the treatment of congestive heart failure. This involved the coordination of biology and chemistry research within Smith Kline in both UK and USA. Two compounds, both selective PDE 3 inhibitors, were selected for development, SK&F 94120 and siguazodan (SK&F 94836). Subsequently initiated and led another major world-wide (Welwyn and Philadelphia) research programme concerned with PDE 5 inhibitors, this is believed to be the first such programme to be established.

1988-1993. Director of Biology R&D at Laboratorios Almirall, Barcelona, Spain. Almirall Prodesfarma is Spain's leading national pharmaceutical company and currently has over 2000 employees. Whilst there, established a number of new research programmes including selective PDE 4 inhibitors, potassium channel activators, CCK antagonists, flosequinan like cardiostimulants (PDE 3 inhibitors), 5HT agonists and antagonists as anxiolytic, anti emetic, gastric prokinetic and anti-migraine agents. Was directly involved in the developments of ebastine and its active metabolite carebastine both non-sedating anti histamines, pancopride a 5HT3 antagonist anti-emetic, LAS Z 019 a 5HT4 agonist, prokinetic agent, LAS 31025, a selective PDE4 inhibitor, which progressed to clinical phase 3 for asthma and chronic obstructive pulmonary disease, and almotriptan, an anti-migraine agent. This included the responsibility for pre-clinical biology studies, including toxicology, DMPK and external pharmacology/biochemistry which were conducted both internally and within contract research organizations and academic institutions world-wide.

1993-1996. Head of Biology R&D at Chiroscience Ltd., Cambridge, U. K. Reporting staff 25 in Biochemistry and Pharmacology departments. As Head of Biology R&D, was responsible for the establishment of biological research and development within the company. This involved the recruitment of research staff and the setting up of the biochemistry and pharmacology laboratories. Was also responsible for Toxicology and DMPK. Initiated and was project leader for the selective PDE 4 inhibitor programme which was successfully out-licensed. Was project leader for the development of Chirocaine (levobupivacaine), a single enantiomer local anaesthetic, through to clinical proof of principle and represented Chiroscience at the presentation to the US FDA advisory committee in January 1999. Chirocaine, which is currently marketed in 20 plus Countries, was the first product from a UK biotech company to be approved in the USA.

1996-Present. Director of Cambridge BioConsultants Ltd., Cambridge U.K. Was founder of the company, which has provided consultancy to a number of clients. This includes advising on pharmacology, DMPK and toxicology studies, the writing of expert reports for drug registration, CTX submissions, Investigators Brochures for clinical studies, presentations to regulatory authorities (in UK and USA) and numerous due diligence studies conducted on behalf of venture capital organizations.

1998-2007. Director of Arachnova Ltd., Cambridge U. K. Was co-founder of the company in 1998. Arachnova Ltd. specialized in the identification of new therapeutic uses for existing drugs.

2000-2007. Director and CSO of Arachnova Therapeutics Ltd., St Helier Jersey. Was co-founder of the company in September 2000. Arachnova Therapeutics was a venture capital

backed pharmaceutical company, which specialized in the development and commercialization of projects largely identified by Arachnova Ltd. The company had a number of projects in the areas of atopic dermatitis, neuropathic pain, urinary incontinence, functional bowel disease, hypertrophic scarring, Dupuytren's contracture and pulmonary fibrosis. The company effectively ceased once Its key projects, related to MCI225, were out-licensed to a 3rd party in 2006-2007.

2007-present CSO Acacia Pharma PLC., Cambridge UK. Was a co-founder of the company. Acacia Pharma is a venture capital backed pharmaceutical company focused on hospital-based supportive care and in particular cancer supportive care. Current clinical development projects are in the areas of post operative nausea and vomiting, chemotherapy induced nausea and vomiting, cancer cachexia and cancer related xerostomia. Responsibilities include project discovery, DMPK and toxicology.

Publications (full papers/ reviews)

1. Characterisation of an isolated working guinea-pig heart including effects of histamine and noradrenaline. Flynn S. B., Gristwood R. W. and Owen D. A. A. (1978). J. Pharmacol. Meth., 1, 183-195.

2. Differentiation of the roles of histamine H1-and H2- receptors in the mediation of the effects of histamine in the working heart of the guinea-pig. Flynn S. B., Gristwood R. W. and Owen D. A. A. (1979). Br. J. Pharmacol, 65, 127-137.

3. Cardiovascular studies with impromidine (SK&F 92676), a new, very potent and specific histamine H2- receptor agonist. Owen D. A. A., Harvey C. A. and Gristwood R. W. (1979). J. Pharm. Pharmacol., 31, 577-582.

4. Effects of histamine on human isolated heart muscle. Comparison with effects of noradrenaline. Gristwood R. W., Lincoln J. C. R. and Owen D. A. A. (1981). Br. J. Pharmacol., 32, 145-146.

5. Histamine release from human right atrium. Gristwood R. W., Lincoln J. C. R., Owen D. A. A. and Smith I. R. (1981). Br J. Pharmacol., 74, 7-9.

6. Response of human ventricular heart muscle to histamine. Gristwood R. W., Owen D. A. A., Eckel L., Satter P. and Nawrath H. (1981). J. Pharm. Pharmacol., 33, 246-247.

7. Inotropic and electrophysiological effects of histamine on human ventricular heart muscle. Eckel L., Gristwood R. W., Nawrath H., Owen D. A. A. and Satter P. (1982). J. Physiol., 330, 111-123.

8. Evidence that oxmetidine inhibits transmembrane calcium flux in cardiac and vascular tissue. Gristwood R. W., Jim K. F., Macia R. W., Matthews W. D., Morl C. J. and Owen D. A. A. (1985). Br. J. Pharmacol., 85, 923-932.

9. Some studies on the release of histamine from mast cells treated with D- tubocurarine. Ali H., Gristwood R. W. and Pearce F. L. (1986). Agents and Actions, 18, 71-73.

10. Pharmacological studies with SK&F 94120 a novel positive inotropic agent with vasodilator activity. Gristwood R. W., Eden R. J., Owen D. A. A. and Taylor E. M. (1986). J. Pharm. Pharmacol., 89, 335-340.

11. Impromidine is a partial agonist on human ventricular myocardium. English T. A. H., Gristwood R. W., Owen D. A. A. and Wallwork J. (1986). Br. J. Pharmacol., 89, 335-340.

12. Analysis of cardiac responses to a selective phosphodiesterase III inhibitor, SK&F 94120, on isolated myocardium including human ventricular myocardium from "end stage" failure patients. Gristwood R. W., English T. A. H., Wallwork J., Sampford K. A. and Owen D. A. A. (1987). J. Cardiovasc. Pharmacol., 9, 719-727.

13. The "ex vivo" effects of thyroid status on atrial and ventricular electrophysiology in rats. Rothaul A. L. and Gristwood R. W. (1988). Can. J. Phys. Pharmacol, 66, 90-94.

14. "In vivo" pharmacology studies with SK&F 94836, a potent inotrope/ vasodilator with a sustained duration of action. Gristwood R. W., Comer M. B., Eden R. J., Taylor E. M., Turner J. A., Wallduck M. and Owen D. A. A. (1988). Br. J. Pharmacol., 93, 893-901.

15. Effects of theophylline compared with prednisolone on late phase airway leukocyte infiltration in guinea-pigs. Gristwood R. W., Llupia J., Fernandez A. G. and Berga P. (1991). Int. Arch. Allergy Appl. Immunol., 94, 293-294.

16. Effects of prednisolone, salbutamol and theophylline on bronchial hyperreactivity and leukocyte chemokinesis in guinea-pigs. Llupia J., Fernandez A. G., Llenas J. and Gristwood R. W. (1991). Drugs Exp. Clin. Res., 17(8), 395-398.

17. Studies on the cardiac actions of flosequinan in vitro. Gristwood R. W., Beleta, J., Bou J., Cardelus I., Fernandez A. G., Llenas J. and Berga P. (1992). Br. J. Pharmacol., 105, 985-991.

18. The calcium channel blocker LAS 30538, unlike nifedipine, verapamil, diltiazem or flunarizine, potently inhibits insulin secretion in rats and dogs. Gristwood R. W., Furman B. L., Llenas J., Jauregui J. and Berga P. (1992). J. Pharm. Pharmacol., 44, 851-855.

19. Cardiovascular effects of LAS 30538, a new vascular selective calcium channel blocker. Cardelus I., Bou J., Llenas J., Berga P. and Gristwood R. W. (1992). J. Pharm. Pharmacol., 44. 830-835.

20. Pancopride, a potent and long-acting 5HT3 receptor antagonist, is orally effective against anticancer drug-evoked emesis. Fernandez A. G., Puig J., Beleta J., Domenech T., Bou J., Berga P., Gristwood R. W. and Roberts D. J. (1992). Eur. J. Pharmacol., 222, 257-264.

21. Investigations into the role of PDE IV in bronchorelaxation including studies with human bronchus. Cortijo J., Bou J., Beleta J., Cardelus I., Llenas J., Morcillo E. and Gristwood R. W. (1993). Br. J. Pharmacol. 108, 562-568.

22. Effectos cardiovasculares de los inhibidores de la fosfodiesterasa. Gristwood R. W. (1993). Excerpta Medica, Investigacion en hipertension, 74-80.

23. Identification and characterization of serotonin 5HT4 receptor binding sites in human brain: comparison with other mammalian species. Domenech T., Beleta J., Fernandez A. G./ Gristwood R. W., Cruz-Sanchez F., Tolsa E. and Palacios J. M. (1994). Mol. Brain Res., 21, 176-180.

24. Mecamylamine reverses physostigmine- induced attenuation of scopolamine- induced hyperactivity. O' Neill M. F., Fernandez A. G., Gristwood R. W. and Palacios J. M. (1994). J. Neural Transm [Gen Sect], 96, 9-18.

25. Meeting of the British Pharmacological Society 5-7th January 1994, London U. K. Gristwood R. W. (1994). Exp. Opin. Invest. Drugs 3 (4): 397-398.

26. Pharmacokinetic studies of pancopride in rat and dog. Martinez-Tobed A., Aubets J., Anton M. J. and Gristwood R. W. (1994). Eur. J. Drug Metab. and Pharmacokinetics, Special Issue participants papers of Proceedings of 5th European Congress of Biopharmaceutics and Pharmacokinetics held in Brussels April 1993.

27. Reduced cardiotoxicity of levobupivacaine compared with racemic bupivacaine (Marcaine): new clinical evidence. Gristwood R. W., Bardsley H., Baker, H. and Dickens J. (1994). Exp. Opin. Invest. Drugs, 3(11), 1209-1212.

28. Pharmacology and toxicological profile of LAS 30538: a new vascular selective calcium channel blocker. Llenas J., Cardelus I., Bou J., Gras J., Jauregui J. Martinez-Tobed A. and Gristwood R. W. (1995). Cardiovascular Drug Reviews, 13 (1) 1-18.

29. Phosphodiesterase (PDE) 4 inhibitors: anti inflammatory drugs of the future? Teixeira M., Gristwood R. W., Cooper N. and Hellewell P. G. (1997). Trends in Pharmacol Sci., 18, 164-168.

30.The local anaesthetic potency of levobupivacaine does not differ from racemic bupivacaine (Marcain): first clinical evidence. Bardsley H, Gristwood R. W., Watson N. and Nimmo W. (1997). Exp. Opin. Invest. Drugs, 3, 1209-1212.

31. A comparison of the inhibitory activity of selective PDE4 inhibitors on eosinophil recruitment in guinea pig skin. Teixeira M. M., Miotla J. M., Cooper N., Gristwood R. W. and Hellewell P. G. (1997). Mem. Inst. Oswaldo Cruz, 92 Suppl 2, 193-196.

32. A comparison of the cardiovascular effects of levobupivacaine and racemic bupivacaine following intravenous administration to healthy volunteers. Bardsley H, Gristwood R. W., Baker H., Watson N. and Nimmo W. (1998). Brit. J. Clin. Pharmacol., 46, 1863-1871.

33. Cardiotoxicity of histamine and the possible role of histamine in the arrhythmogenesis produced by certain antihistamines. Llenas J., Cardelus I., Heredia A., de Mora F. and Gristwood R. W. (1999). Drug Saf. 21 Suppl, 33-38.

34. A comparison of the inhibitory activity of PDE4 inhibitors on leucocyte PDE4 activity in vitro and eosinophil trafficking in vivo. Cooper N., Teixeira M. M., Warneck J., Wills R. E., Macari D. M., Gristwood R. W. and Helliwell P. G. (1999). Br. J. Pharmacol. 126, 1863-1871.

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