

Spedding Research Solutions SARL

Michael Spedding, PhD, FBPharmacS, Chair NC-IUPHAR

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Activities of Spedding Research Solutions SARL Active from 1st June 2013-present.

Location : 6 Rue Ampere, Le Vésinet, 78110, France. Website :

www.speddingresearchsolutions.fr

Turnover 2014: 250,000€, declared profit 3,700€.

Publications are in Appendix 1. Meetings/conferences in Appendix 2.

Other offices/activities :

- **Consultant, Servier, half time (May 2013-May 2016).** Innumerable reports and meetings, analysis of new opportunities for Servier, participation at Servier meetings. Organise ANMI and other research meetings.
- **Office at Hopital Sainte Anne, collaborations in psychiatry.**
- **Work package Leader: Innovative Medicines Initiatives (IMI) : Newmeds (psychiatry), a multinational consortium in psychiatry research (finishing this year).**
- **Honorary Professor University of Edinburgh.** Coholder of 540,00£/3 years grant from Wellcome Foundation employing 5 curators to maintain the IUPHAR/BPS guidetopharmacology.org knowledgebase, a guide to all the drug sites encoded by the human genome. Website visited by scientists from 160 countries. Have just won a 450,000€ immunopharmacology grant
- **Ex-Chair Nomenclature Committee of International Union of Pharmacology.** Two meetings (20 people)/year at Edinburgh and Paris. Coordination of 90 expert subcommittees of 700 scientists who freely give time to curate data in the IUPHAR/BPS guidetopharmacology.org. Furthermore, this committee has published >100 publications in the last 21 years (during which time I was secretary or chair), and the publications have been very highly cited (H-index 74). UNESCO in a review stated that this activity had “real implications for improvement of human well-being, wealth creation, and exploration of natural and traditional medicines from the developing world”
- **Secretary General of International Union of Pharmacology (charity based in Switzerland, offices in Kansas City) from July 2013 at the World Congress in Cape Town.** Reports to International Council of Scientific Unions (ICSU) and then to UNESCO. Coordination of activities of the world’s pharmacology societies, and IUPHAR sections. Raise funds and coordinate activities. *Initiatives:* natural products (China, India), Immunopharmacology, Aging Research, Initiative for Africa (example, free access to scientific publications in Africa). Precompetitive data sharing of new breakthroughs in science.
- **Five times fastest, M 65-70, at 5000m parkruns. Four times in top 3 fastest at trackdays with my Opel Speedster turbo (>50 cars).** Support: Garage Sport AUTO 3000 (José Martens, ex-mechanic of Sebastien Loeb and Renault F1)

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Research Activities.

As opposed to normal academic research, or industrial research, the main objective is to define and mitigate key 'roadblocks' to the main problems in drug discovery and development and healthcare and help resolve them with expert meetings followed by expert-based recommendations, or by sharply-defined experiments. These questions are very high level integrating widely different approaches which have not been put together before.

1. **Amyotrophic lateral sclerosis (ALS).** This terrible disease neurodegenerative disease affects ~8000 people per year in France, with virtually no therapy. This project is going fast and we now have evidence that the enzymes involved in glycosphingolipid metabolism may be causal in the disease and precipitate in granules with TDP-43 in ALS patients. This may allow new therapies and explain the hypermetabolism, neuronal retraction and autophagy in ALS, allowing new perspectives for therapies. We have a hypothesis for the disease which we are testing. A consortium of the Universities of Oxford, Cork and Strasbourg works well.

The consortium has got a grant from Target ALS for ~100K\$ for two years for the background research (I am consultant and unpaid participant to this grant), which allows SRS to concentrate on the industrial aspects and the effects of enzyme modulators.

Servier funding to continue this research (Sept 2014 – Sept 2015, with one year continuation). Three subcontracts with the Universities of Oxford, Strasbourg and Cork complete and new program proposed for partners (plus chemistry) for Sept 2015-2016.

A stagiaire helps with the research literature.

2. **Neuroinflammation.** This project is going more slowly due to few funds, but I have some grant applications under review. We have started an IUPHAR immunopharmacology group and obtained 400K€ IUPHAR funding.
3. **Ageing molecular mechanisms, and sports. IRMES collaboration.** Link IUPHAR gerontology research section, and IRMES - scientific branch of INSEP (plenary lecture, PhD student).
4. **Recent Human Evolution and Modern Diseases.** Grant under review. Background research on how human evolution to run (skeleton, brain, muscle) over <1million years increased oxidative metabolism 3-fold, and the over 100,000 years we evolved to fill all the niches of the planet. We define and prioritise the molecular determinants of this recent evolution, and effects in molecular diseases.
5. **IUPHAR** : coordination of activities on the drug binding sites in the human genome and production of papers by world experts on **what we know and don't know** in the areas of disease ontologies and the new areas of alternative splicing, allostereism, non-coding RNAs, immunopharmacology etc.
6. **Psychiatry.** We have defined **the key circuits involved in psychiatric disorders and drugs which may impact these circuits.** These circuits will have developed during recent human evolution. We have new hypotheses to describe how this occurred and the implications for modern diseases. Validated by IMI-Newmeds.

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Company Organisation

Accountant: Thibault Gianati

Computing: Contract with Servinf (J-L Remond)

Web services : J Maurin (autoentrepreneur)

Insurance : Cabinet Jalouneix

Legal : Sarah M'Sallah.

Employees (to September, 2015):

Assistant (à distance) : Martine Gruelle

Stagiaire : Imen Dahbi

Appendix 1. Full Publications (congress abstracts not listed).

Editor:

1. Special Issue, British Journal of Pharmacology : "Mitochondrial Pharmacology: Energy, Injury & Beyond". 2013.
2. Concise Guide to Pharmacology, British Journal of Pharmacology.

Thirty full scientific publications listed by Pubmed from Spedding Research Solutions since its formation (2013-March 2015).

2014: Named in top 82 most cited French scientists (top 3000 world) of all scientific disciplines (topcited.com). I am the only industrial scientist in the French list.

Listed among 'world's most influential scientific minds 2014' by Thomson Reuter's, from LLS.

1: Babbitt PC, Bagos PG, Bairoch A, Bateman A, Chatonnet A, Chen MJ, Craik DJ, Finn RD, Gloriam D, Haft DH, Henrissat B, Holliday GL, Isberg V, Kaas Q, Landsma D, Lenfant N, Manning G, Nagano N, Srinivasan N, O'Donovan C, Pruitt KD, Sowdhamini R, Rawlings ND, Saier MH Jr, Sharman JL, Spedding M, Tsigos KD, Vastermark A, Vriend G. Creating a specialist protein resource network: a meeting report for the protein bioinformatics and community resources retreat. Database (Oxford). 2015 Jul 11;2015:bav063. doi: 10.1093/database/bav063. eCollection 2015. PubMed PMID: 26284514; PubMed Central PMCID: PMC4499208.

2: Grimm O, Gass N, Weber-Fahr W, Sartorius A, Schenker E, Spedding M, Risterucci C, Schweiger JI, Böhringer A, Zang Z, Tost H, Schwarz AJ, Meyer-Lindenberg A. Acute ketamine challenge increases resting state prefrontal-hippocampal connectivity in both humans and rats. Psychopharmacology (Berl). 2015 Jul 18. [Epub ahead of print] PubMed PMID: 26184011.

3: Tiligada E, Ishii M, Riccardi C, Spedding M, Simon HU, Teixeira MM, Landys Chovel Cuervo M, Holgate ST, Levi-Schaffer F. The expanding role of immunopharmacology: IUPHAR Review 16. Br J Pharmacol. 2015 Sep;172(17):4217-27. doi: 10.1111/bph.13219. Epub 2015 Jul 21. PubMed PMID: 26173913.

4: Ling I, Mihalik B, Etherington LA, Kapus G, Pálvölgyi A, Gigler G, Kertész S Gaál A, Pallagi K, Kiricsi P, Szabó É, Szénási G, Papp L, Hársing LG, Lévy G, Spedding M, Lambert JJ, Belelli D, Barkóczy J, Volk B, Simig G, Gacsályi I, Antoni FA. A novel GABA(A) alpha 5 receptor inhibitor with therapeutic potential. Eur J Pharmacol. 2015 Jul 11;764:497-507. doi: 10.1016/j.ejphar.2015.07.005. [Epub ahead of print] PubMed PMID: 26169564.

5: Holliday GL, Bairoch A, Bagos PG, Chatonnet A, Craik DJ, Finn RD, Henrissat B, Landsman D, Manning G, Nagano N, O'Donovan C, Pruitt KD, Rawlings ND, Saier M, Sowdhamini R, Spedding M, Srinivasan N, Vriend G, Babbitt PC, Bateman A. Key challenges for the creation and maintenance of specialist protein resources. Proteins. 2015 Jun;83(6):1005-13. doi: 10.1002/prot.24803. Epub 2015 Apr 22. PubMed PMID: 25820941; PubMed Central PMCID: PMC4446195.

6: Tripathi A, Schenker E, Spedding M, Jay TM. The hippocampal to prefrontal cortex circuit in mice: a promising electrophysiological signature in models for psychiatric disorders. Brain Struct Funct. 2015 Mar 12. [Epub ahead of print] PubMed PMID: 25761930.

Société à Responsabilité Limitée au capital de 25,000 € ; Gérant : Michael Spedding; courriel : michael@speddingresearchsolutions.fr
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7: Godsil BP, Bontempi B, Mailliet F, Delagrangé P, Spedding M, Jay TM. Acute tianeptine treatment selectively modulates neuronal activation in the central nucleus of the amygdala and attenuates fear extinction. *Mol Psychiatry*. 2015 Jan 6. doi: 10.1038/mp.2014.169. [Epub ahead of print] PubMed PMID: 25560759.

8: Christopoulos A, Changeux JP, Catterall WA, Fabbro D, Burris TP, Cidlowski JA, Olsen RW, Peters JA, Neubig RR, Pin JP, Sexton PM, Kenakin TP, Ehlert FJ, Spedding M, Langmead CJ. International Union of Basic and Clinical Pharmacology. XC. multisite pharmacology: recommendations for the nomenclature of receptor allosterism and allosteric ligands. *Pharmacol Rev*. 2014 Oct;66(4):918-47. doi: 10.1124/pr.114.008862. PubMed PMID: 25026896.

9: Markham A, Bains R, Franklin P, Spedding M. Changes in mitochondrial function are pivotal in neurodegenerative and psychiatric disorders: how important is BDNF? *Br J Pharmacol*. 2014 Apr;171(8):2206-29. doi: 10.1111/bph.12531. Review. PubMed PMID: 24720259; PubMed Central PMCID: PMC3976631.

10: Davidson SM, Lopaschuk GD, Spedding M, Beart PM. Mitochondrial pharmacology: energy, injury and beyond. *Br J Pharmacol*. 2014 Apr;171(8):1795-7. doi:10.1111/bph.12679. PubMed PMID: 24684388; PubMed Central PMCID: PMC3976605.

11: Zohar J, Nutt DJ, Kupfer DJ, Moller HJ, Yamawaki S, Spedding M, Stahl SM. A proposal for an updated neuropsychopharmacological nomenclature. *Eur Neuropsychopharmacol*. 2014 Jul;24(7):1005-14. doi:10.1016/j.euroneuro.2013.08.004. Epub 2013 Sep 18. PubMed PMID: 24630385.

12: Alexander SP, Benson HE, Faccenda E, Pawson AJ, Sharman JL, Spedding M, Peters JA, Harmar AJ; CGTP Collaborators. The Concise Guide to PHARMACOLOGY 2013/14: transporters. *Br J Pharmacol*. 2013 Dec;170(8):1706-96. doi: 10.1111/bph.12450. PubMed PMID: 24528242; PubMed Central PMCID: PMC3892292.

13: Alexander SP, Benson HE, Faccenda E, Pawson AJ, Sharman JL, Spedding M, Peters JA, Harmar AJ; CGTP Collaborators. The Concise Guide to PHARMACOLOGY 2013/14: catalytic receptors. *Br J Pharmacol*. 2013 Dec;170(8):1676-705. doi: 10.1111/bph.12449. PubMed PMID: 24528241; PubMed Central PMCID: PMC3892291.

14: Alexander SP, Benson HE, Faccenda E, Pawson AJ, Sharman JL, Spedding M, Peters JA, Harmar AJ; CGTP Collaborators. The Concise Guide to PHARMACOLOGY 2013/14: nuclear hormone receptors. *Br J Pharmacol*. 2013 Dec;170(8):1652-75. doi: 10.1111/bph.12448. PubMed PMID: 24528240; PubMed Central PMCID: PMC3892290.

15: Alexander SP, Benson HE, Faccenda E, Pawson AJ, Sharman JL, Catterall WA, Spedding M, Peters JA, Harmar AJ; CGTP Collaborators. The Concise Guide to PHARMACOLOGY 2013/14: ion channels. *Br J Pharmacol*. 2013 Dec;170(8):1607-51. doi: 10.1111/bph.12447. PubMed PMID: 24528239; PubMed Central PMCID: PMC3892289.

16: Alexander SP, Benson HE, Faccenda E, Pawson AJ, Sharman JL, Spedding M, Peters JA, Harmar AJ; CGTP Collaborators. The Concise Guide to PHARMACOLOGY 2013/14: ligand-gated ion channels. *Br J Pharmacol*. 2013 Dec;170(8):1582-606. doi: 10.1111/bph.12446. PubMed PMID: 24528238; PubMed Central PMCID: PMC3892288.

17: Alexander SP, Benson HE, Faccenda E, Pawson AJ, Sharman JL, McGrath JC, Catterall WA, Spedding M, et al., The Concise Guide to PHARMACOLOGY 2013/14: overview. *Br J Pharmacol*. 2013 Dec;170(8):1449-58. doi: 10.1111/bph.12444. PubMed PMID: 24528237; PubMed Central PMCID: PMC3892286.

18: Alexander SP, Benson HE, Faccenda E, Pawson AJ, Sharman JL, Spedding M, Peters JA, Harmar AJ; CGTP Collaborators. The Concise Guide to PHARMACOLOGY 2013/14: G protein-coupled receptors. *Br J Pharmacol*. 2013 Dec;170(8):1459-581. doi: 10.1111/bph.12445. PubMed PMID: 24517644; PubMed Central PMCID: PMC3892287.

19: Pawson AJ, Sharman JL, Benson HE, Faccenda E, Alexander SP, Buneman OP, Davenport AP, McGrath JC, Peters JA, Southan C, Spedding M, Yu W, Harmar AJ; NC-IUPHAR. The IUPHAR/BPS Guide to PHARMACOLOGY: an expert-driven knowledgebase of drug targets and their ligands. *Nucleic Acids Res*. 2014 Jan;42(Database issue):D1098-106. doi: 10.1093/nar/gkt1143. Epub 2013 Nov 14. PubMed PMID: 24234439; PubMed Central PMCID: PMC3965070.

20: Alexander SP, Benson HE, Faccenda E, Pawson AJ, Sharman JL, Spedding M, Peters JA, Harmar AJ; CGTP Collaborators. The Concise Guide to PHARMACOLOGY 2013/14: enzymes. *Br J Pharmacol*. 2013 Dec;170(8):1797-867. doi: 10.1111/bph.12451. PubMed PMID: 24528243; PubMed Central PMCID: PMC3892293.

21: Gass N, Schwarz AJ, Sartorius A, Schenker E, Risterucci C, Spedding M, Zheng L, Meyer-Lindenberg A, Weber-Fahr W. Sub-anesthetic ketamine modulates intrinsic BOLD connectivity within the hippocampal-prefrontal circuit in the rat. *Neuropsychopharmacology*. 2014 Mar;39(4):895-906. doi: 10.1038/npp.2013.290. Epub 2013 Oct 18. PubMed PMID: 24136293; PubMed Central PMCID: PMC3924524.

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22: Schwarz AJ, Gass N, Sartorius A, Risterucci C, Spedding M, Schenker E, Meyer-Lindenberg A, Weber-Fahr W. Anti-correlated cortical networks of intrinsic connectivity in the rat brain. *Brain Connect*. 2013;3(5):503-11. doi: 10.1089/brain.2013.0168. Epub 2013 Sep 26. PubMed PMID: 23919836; PubMed Central PMCID: PMC3796325.

23: Davenport AP, Alexander SP, Sharman JL, Pawson AJ, Benson HE, Monaghan AE, Liew WC, Mpamhanga CP, Bonner TI, Neubig RR, Pin JP, Spedding M, Harmar AJ. International Union of Basic and Clinical Pharmacology. LXXXVIII. G protein-coupled receptor list: recommendations for new pairings with cognate ligands. *Pharmacol Rev*. 2013 May 17;65(3):967-86. doi: 10.1124/pr.112.007179. Print 2013 Jul. Review. PubMed PMID: 23686350; PubMed Central PMCID: PMC3698937.

24: Guesdon V, Malpoux B, Delagrangre P, Spedding M, Cornilleau F, Chesneau D, Haller J, Chaillou E. Rapid effects of melatonin on hormonal and behavioural stressful responses in ewes. *Psychoneuroendocrinology*. 2013 Aug;38(8):1426-34. doi: 10.1016/j.psyneuen.2012.12.011. Epub 2013 Jan 20. PubMed PMID: 23337408.

25: Godsil BP, Kiss JP, Spedding M, Jay TM. The hippocampal-prefrontal pathway: the weak link in psychiatric disorders? *Eur Neuropsychopharmacol*. 2013 Oct;23(10):1165-81. doi: 10.1016/j.euroneuro.2012.10.018. Epub 2013 Jan 15. Review. PubMed PMID: 23332457.

26: Schwarz AJ, Gass N, Sartorius A, Zheng L, Spedding M, Schenker E, Risterucci C, Meyer-Lindenberg A, Weber-Fahr W. The low-frequency blood oxygenation level-dependent functional connectivity signature of the hippocampal-prefrontal network in the rat brain. *Neuroscience*. 2013 Jan 3;228:243-58. doi: 10.1016/j.neuroscience.2012.10.032. Epub 2012 Oct 23. PubMed PMID: 23098800.

27: Sharman JL, Benson HE, Pawson AJ, Lukito V, Mpamhanga CP, Bombail V, Davenport AP, Peters JA, Spedding M, Harmar AJ; NC-IUPHAR. IUPHAR-DB: updated database content and new features. *Nucleic Acids Res*. 2013 Jan;41(Database issue):D1083-8. doi: 10.1093/nar/gks960. Epub 2012 Oct 18. PubMed PMID: 23087376; PubMed Central PMCID: PMC3531077.

28: Gacsályi I, Nagy K, Pallagi K, Lévy G, Hársing LG Jr, Móricz K, Kertész S, Varga P, Haller J, Gigler G, Szénási G, Barkóczy J, Bíró J, Spedding M, Antoni FA. Egis-11150: a candidate antipsychotic compound with procognitive efficacy in rodents. *Neuropharmacology*. 2013;64:254-63. doi: 10.1016/j.neuropharm.2012.07.017. Epub 2012 Jul 21. PubMed PMID: 22824189.

29: Zhang H, Etherington LA, Hafner AS, Belelli D, Coussen F, Delagrangre P, Chaouloff F, Spedding M, Lambert JJ, Choquet D, Groc L. of AMPA receptor surface trafficking and synaptic plasticity by a cognitive enhancer and antidepressant molecule. *Mol Psychiatry*. 2013 Apr;18(4):471-84. doi: 10.1038/mp.2012.80. Epub 2012 Jun 26. PubMed PMID: 22733125; PubMed Central PMCID: PMC3606944.

30. **引用** | Michael SPEDDING. 药理学学会, 药理学与天然产物. *中国药理学与毒理学杂志*, 2015, 29 (S1): 3-4.

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Appendix 2. Participation at Scientific Conferences/Work packages

2013

June – 1 week, Research Fellow at Oxford, MRC Pharmacology

September : Alzheimer Drug Discovery Foundation – New York,

European College of Neuropsychopharmacology, (ECNP) Barcelona (plenary)

October NC-IUPHAR – Paris,

November : American Society of Neurosciences (+ Newmeds meeting), San Diego,

December : British Pharmacological Society, London

Three research meetings at Strasbourg (ALS)

Seven congress presentations.

2014

January Newmeds meeting Basle,

Jan : Wellcome Grant Holders Meeting Edinburgh (also June, October, plus IUTOX meeting, Glasgow)

April NC-IUPHAR Meeting Edinburgh

July World Congress of Pharmacology, Cape Town (**plenary, organiser**)

Invited lecture IOP September, London

Invited lecture, Groupe de Recherche en Psychiatrie Saint Malo October

Invited lecture SRIMC Budapest October

October ECNP meeting Berlin

October NC-IUPHAR Meeting Paris

November : American Society of Neurosciences (+ Newmeds meeting), Washington,

December : British Pharmacological Society, London

Three meetings at Strasbourg (ALS)

~7 congress presentations

2015.

Jan : Wellcome Grant Holders Meeting Edinburgh (also June, October)

Wellcome Trust Strategy meeting, London

Invited lecture, University of Durham

Newmeds Meeting London

Edinburgh NC-IUPHAR, April 17-19 (**organiser**), +BPS Drug discovery meeting

ASCEPT/BPS Meeting Hong Kong, (plenary) May 20-23, + IUPHAR exec comm Xi'An China (**organiser**)

1 Day GeNeuro Meeting at Lyon.

Poland, 1 week Research June

IUPHAR Singapore Natural Products 22-24 July (plenary)

IRMES (INSEP) Annual meeting (plenary) September, Orleans

Servier ANMI meeting (**organiser**) 8-10 October Chantilly

Servier Protein splicing meeting (**organiser**) November

ECNP August Amsterdam

NC-IUPHAR : 23-25 October Paris (**organiser**)

Indian Pharmacology Society 2015, December (plenary)

10 congress presentations.



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