François IRIS

Scientific Profile

Dr François Iris has an unusual track record characterised by an uncommon ability to rapidly and successfully reach well beyond the current state of the art to implement paradigm shifts in multiple pluri-disciplinary scientific domains. He left school in France at age 14 to become an apprentice cook. For the next 14 years he worked in restaurants throughout Europe and in New Zealand where he migrated in 1976. At age 27, while still working as a chef, he resumed high school and, a University Entrance diploma in hand, took undergraduate courses in biology and biochemistry (1979).

He graduated with 1st class honours in Animal Physiology (1982) and obtained a Ph.D. in Zoology (Physiology/Genetics/Biochemistry; 1985).

Immediately recruited by the University of Otago (1985), he joined the Endocrinology Section in the Dept. of Medicine (lecturer grade) at the Christchuch School of Medicine where he created and led a small group working on the molecular biology of autoimmune diseases (diabetes & multiple sclerosis) (1-3). He competed for the highly regarded "Medical Research Council Post-Doctorate Fellowship Award" and won one of the two awards granted yearly nationwide (1986). He then became the scientific coordinator of the Cell Biology Group in the Dept of Medicine and the thesis director of two Ph.D. students, both of whom graduated and went on to pursue successful academic careers.

Three years later, Prof. Jean Dausset (Nobel Laureate in Medicine, 1980), invited him to join his staff as group leader at the CEPH in Paris. Prior to leaving New Zealand, he competed for and won the prestigious "Medical Research Council Overseas Fellowship Award" (one fellowship every second year nationwide; 1989).

Within less than six months after his arrival at the CEPH, he had created and was leading a high-throughput DNA sequencing unit, which became one of the most respected in Europe, involved in the international Human Genome collaborative project. The major successes of his team (Oct. 1989 – June 1993) include the discovery of the glucokinase gene mutations associated with the MODY-2 form of diabetes (4*); the genomic sequencing and assembly of the entire TNF region (170 kb) in the human HLA class III locus and the discovery of a new gene homologous to NFkB (5*); the assembly of the entire HLA region (4,5 Mb) (6); the invention and development of numerous new sequencing techniques (7*) and a major contribution to the elaboration of the first physical map of the human genome (8). These were his last years in the academic world.

In June 1993, Dr Iris was approached by prof Eric Lander (Director of the Whitehead Institute, MIT) to become the Director of the DNA sequencing Dept. at Millennium Pharmaceuticals, a biotech firm being created in the USA. The job proposed was to create from scratch and in less than two years what was to be the largest high-throughput DNA sequencing unit in the USA. He arrived in Cambridge (MA) in July 1993 and, by December of that year, the sequencing unit was fully operational, with a weekly output of 550 kilobases of high quality sequence data (the highest in the USA) encompassing all forms of DNA sequencing and data analyses. This achievement lead to a 75 M$ collaboration contract with the Swiss pharmaceutical firm Hoffman-LaRoche (Sept 94), the second largest deal in the history of US biotechnology at the time. One of the Dept's major successes (Jan.–Dec.94) was the discovery of PKD1, responsible for polycystic kidney disease, the identification of the protein's functions and the disease-causing mutations (9*).

It is during this period that Dr Iris started developing the methodologies and tools that would become the basis for one form of Systems Biology. His first efforts in this field (Dec. 94-Aug. 95) led to the discoveries of the UCP2 gene, involved in energy metabolism in the context of obesity and diabetes (10), and the involvement of EST1 in a murine form of pseudo-gestational diabetes.

Unable to obtain the means to develop these novel approaches at Millennium, he returned to France to create, together with investors, a biotechnology company dedicated to "Integrative Biology".

ValiGen was created in Paris in June 1996. To first secure the future of this enterprise, Dr Iris recruited a team to develop the novel gene-expression and genotyping technologies he had envisaged while still in the USA, culminating with 3 international patents in analytical molecular biology (US patents n° 6,221,585; 6,403,309 & 6,420,111). He then started developing a computer-assisted integrative analytical process, rewarded by the award of the European Eurekâ label (2000)

and a development grant in excess of 18 M Euro (EUREKA project E!2243). The work of his team resulted in an analytical platform (BioPath™), allowing to efficiently model complex biological phenomena and identify potential therapeutic interventions. Breast cancer progression (11*) and resistance to tamoxifen therapy (12*, 13*) were amongst the major achievements, involving the supervision of a Ph.D student who participated actively and graduated "cum laudae". By then, ValiGen had become an international group employing over 180 researchers and technicians. But Dr Iris remained dissatisfied with the modelling approaches developed that did not allow to model in actual physiological contexts. Concurrently, he was in deep disagreement with investors over the forms of development they were imposing upon ValiGen. In December 2001, Dr Iris left the company he had co-created and made scientifically very successful and well respected internationally.

He then took time to think-out approaches whereby physiologically valid predictive biological modelling could be undertaken as well as means that would allow to create and sustain a biotech entity dedicated to Systems Biology without recourse to external investors. In this, he found considerable help in four professionals with significant experience in private enterprises, management and technology transfers (Mrs Gea, Santamaria and Lampe, engineering scientists and computing specialists from Ecole Centrale and Prof Dine, a highly respected haematologist and technology specialist). All five decided to join forces and devised a novel strategy for the creation of a biotech enterprise entirely free from venture capital interference while Dr Iris started developing a new approach to Systems Biology (the CADI™ platform) allowing accurate, physiologically valid, multi-scale predictive modelling, the first version of which became operational in March 2004 (less than 2 years). Bio-Modeling Systems (BMSystems) was created a few weeks prior to signing its first industrial contract with a major pharmaceutical firm (Sept. 2004). Since then, BMSystems has accumulated successes, both industrially and in academic collaborations. An internal research program on the means to control uncharacterised multi-resistant bacterial pathogens without recourse to antibiotics nor vaccines, led to the direct invention and development of three novel technologies (patents WO/2008/093009; WO/2008/093010 & WO/2009/090081) and the creation, in 2007, of a fully financed bio-pharma company (Pherecydes Pharma) controlled at 40% by BMSystems, awarded a grant by the Oséo Innovation Agency and currently in phase of commercial production (14*). A collaborative program with the CEA on the mechanisms of pathogenesis and disease progression of a neurodegenerative disorder (Creutzfeldt-Jakob disease), rewarded by an "Industrial Best Practice Award" granted by the Cambridge Healthtech Institute (USA), led to the direct discovery of new therapeutics for the treatment of psychiatric disorders (patent WO/2010/029131 A1, co-owned by the CEA & BMSystems) and the development of a new bio-pharma entity (TheraNexus). Work with the Max Plank Institute for Psychiatry (München) on the systems biology of anxiety led to the publication of a highly successful scientific volume (15*). Work with the Inserm Unit U493 led to the elucidation of a developmental process (regression of the Müllerian duct) that had remained largely obscure for over 60 years (16*), etc.

Overall, Dr Iris has consistently shown a remarkable capacity to successfully generate innovations, opening new and fruitful research avenues in multiple biological domains. Endowed with a broad and profound multi-disciplinary scientific culture, his communicative enthusiasm, rigorous intellectual honesty and capacity to calmly face and overcome difficulties have played major roles in the constitution and cementing of the many highly productive teams he has created and lead over the years. These qualities, recognised by numerous peers, have led, over the past 8 years, to his continuous renewal as a teacher at some of the most prestigious universities in France (ESPCI, ENSCP, Inserm School, etc.). Highly receptive to collaborative approaches, his clear vision of future scientific and industrial trends has led him to consistently take calculated risks to design, create and implement innovative means to effectively proceed and timely meet anticipated requirements.

References cited above

(1) Scott RE et al. Diabetes Res. Clin. Pract. 2:359-364, 1986; (3) Iris F & Hickford JGH: Détermination des patrons d'empreintes génomiques à loci multiples. In "Jumeaux et sclérose en plaques", 1993 ; (6) Abderhaim H et al. Genomics 23: 520-527, 1994; (8) Bellanne-Chantelot C et al. Cell 70:1059-68, 1992. (10) Gimeno RE et al. Diabetes 46: 900-906, 1997. * : see corresponding numbers (x*) in CV below.

Curriculum Vitae

Francois J-M Iris : Born 30/10/1950, Etival-Clairefontaine, France. francois.iris@bmsystems.net

Education: University of Canterbury (NZ)

1979-1982: B.Sc. (1st class Hon) Comparative Physiology / Neurophysiology

1982-1985: Ph.D. (Zoology) Genetics/ Physiology/ Biochemistry

Professional appointments

- University of Otago, Christchurch Hospital & The Christchurch School of Medicine (NZ)

1985-1986: Research scientist, Dept. of Nuclear Medicine, Christchurch Hospital;

1986-1988: MRC Postdoctoral Fellow, Dept. of Medicine, The Christchurch School of Medicine;

1988-1989: Research Fellow (lecturer) Dept. of Medicine;

- Centre d'Etude du Polymorphisme Humain (CEPH, France)

1989-1993: Team Leader, DNA Sequencing Laboratory (Human Genome Collaborative Project)

- Millennium Pharmaceuticals (USA)

1993-1995: Director, DNA Sequencing Dept.

- ValiGen (France & USA)

1996-2001: Co-founder and Vice-President Science & Technology

- Bio-Modeling Systems (France)

2002-Present: Founder, Chairman and Chief Scientific Officer

Distinctions & Awards

- First Class Honours in Animal Physiology, 1982
- Medical Research Council Postdoctoral Fellow, 1986-88
- Medical Research Council Overseas Fellow, 1989-Present.
- Bio IT World "Best Practice Award" (USA, 2009) for work on Creutzfeldt-Jakob disease.

Teaching & Review Boards

Lecturer on "Complex Biological Systems Analysis":

- Ecole Centrale de Paris (2002-2006);
- Institut Supérieur de Technologie et Management (2003-2009);
- Ecole Nationale Supérieure de Chimie de Paris (2003-2011);
- Ecole Supérieure de Chimie et de Physique Industrielle (2004-2012);
- Ecole de l'INSERM (UE Signalisation Cellulaire) (2006-);
- Evaluation committee of the funding priorities in the Medical Systems Biology "MedSys" program, German Federal Ministry of Research, Berlin (2008-);
- Expert European Commission (2010-).

Affiliations

- Member: Centrale-Santé's directorship committee (2002-)
- Member: Biotechnology Industry Organization (USA) (2008-).
- President of the Scientific Advisory Board, Pherecydes Pharma (2007-2009)

Patents

- US 6,221,585: Method for identifying genes underlying defined phenotypes. Iris F, 1998.
- US 6,403,309: Methods for detection of nucleic acid polymorphisms using peptide-labeled oligonucleotides and antibody arrays. Iris F, 1999;
- US 6,420,111: Multiplex VGID; Iris F, 1999;
- WO/2008/093010: Methods for the concurrent random modification of multiple coding regions within a gene while preserving intact multiple domains within the same gene. Iris, F., 2006;
- WO/2008/093009: Methods for the production of bacteriophages modified by insertion of randomly modified sequences in their host-targeting proteins. Iris F, 2006;
- WO/2009/090081: Modification of the genome of an obligate lytic bacteriophage by immobilisation within its bacterial host. Pouillot F & Iris F, 2008;
- WO/2010/029131 A1: Utilisation of anti-connexin agents to modify the therapeutic effects of psychotropic molecules. Mouthon F, Charveriat M, Delys J-P & Iris F, 2009.

Major Research Publications (total of 19)

-Vionnet N, Stoffel N, Takeda K, Bell GI, Zouali H, Lesage S, Velho G, Passa PH, Iris F, Froguel P, and Cohen D. (1992) Nonsense mutation in the glucokinase gene causes early onset non-insulindependent diabetes mellitus. Nature, 356:721-722. (4*)

-Iris F, Bougueleret L, Prieur S, Rodriguez-Tome P, Caterina, D, Perrot V, Primas G, Dausset J and Cohen D.(1993) Dense Alu clustering and a potential new member of the NF kappa B family within a 90 kilobase HLA class III segment. Nature Genet. 3:137-145. (5*)

-Glücksmann-Kuis MA, Iris F, Tyber O, Woolf EA, Bougueleret L, Deng N, Alperin GD, Hawkins F, Munro C, Lakey N, Duyk G, Schneider MC, Geng L, Zhang F, Zhao Z. et al (1995) Polycystic Kidney Disease: the complete structure of the PKD1 gene and its protein. Cell 81:289-298. (9*)

-Gadal F, Bozic C, Pillot-Brochet C, Malinge S, Wagner S, Le Cam A, Buffat L, Crepin M and Iris F. (2003) Integrated transcriptome analysis of the cellular mechanisms associated with Ha-ras-dependent malignant transformation of the human breast epithelial MCF-7 cell-line. NAR. 39:5789-5804. (11*)

-Gadal F, Bozic C, Pillot-Brochet C, Malinge S, Wagner S, Le Cam A, Vicenzi J, Buffat L, Perret G, Iris F and Crepin M. (2005) Integrative analysis of gene expression patterns predicts specific modulations of defined cell functions by estrogen and tamoxifen in MCF7 cells. JMol.Endocrinol.34:61-75.(12*)

-Iris F, Gea M, Lampe PH and Santamaria P.(2009) Production and implementation of predictive biological models. Med Sci. 25: 608-16. (16*)

-Pouillot F, Blois H & Iris F (2010) Genetically engineered virulent phage banks in the detection and control of emergent pathogenic bacteria. Biosecur Bioterror. 8:155-69. (14*)

Book Chapters & Reviews (total of 8):

- Iris F, Scott RS and Mann JI: Genetic factors in Diabetes Mellitus. In "Clinical Diabetes Mellitus, a problem-oriented approach." 2d edition. JK Davidson, Ed., pp 58-67, Thieme Medical Publishers Inc. New York,1991. (2*)

- Iris F: Optimised methods for large scale shot-gun DNA sequencing in Alu-rich genomic regions. In "Automated DNA sequencing and analysis." M.D Adams, C Field and J.C. Venter Eds., pp 199-209, Academic Press Ltd, 1993. (7*)

- Gadal F, Bozic C, Pillot-Brochet C, Malinge S, Wagner S, Le Cam A, Vicenzi J, Buffat L, Perret G, Iris F and Crepin M. Identification and computer-assisted integration into biological pathways of modulated gene expressions patterns. In "Bioinformatics: New Research", Volume 1. Yan P.V Ed., pp 81-100. Nova Science Publishers, New York, 2005 (13*).

- Iris F: Biological modelling in the discovery and validation of cognitive dysfunctions biomarkers. In "Biomarkers for psychiatric disorders". C.W. Turck Ed., pp 473-522. Springer, New York, 2008. (15*)

-Türck CW and Iris F. Proteome-Based Pathway Modelling of Psychiatric Disorders. Pharmacopsychiatry. 2011; 44 Suppl 1:S54-61.

Iris F: Psychiatric Systems Medicine: Closer at Hand than Anticipated but not with the Expected Portrait. Pharmacopsychiatry. 2012; 45 Suppl 1:S12-21.

International Conferences: *Invited Speaker/Session Chairman* (end 2005-Present only).

2005: Metabolic Profiling, 6th annual conference. 9th December 2005, Orlando, USA. "Integrative Analysis of Complex Physiological Networks".

2006: Drug Discovery Technology Europe, 10th annual conference. 13th-16th March 2006, London, UK. "Predictive Integrative Biology and downstream experimental testing".

2006: Beyond Genome. 19th-21st June 2006, San Francisco, USA. "Predictive Integrative Biology and Downstream Experimental Testing: A Synergistic Paradigm that Deciphers Complex Pathological Processes and Modes of Drug Action".

2007: Max Planck Institute Symposia. 21St January 2007, München, Germany. "Predictive biological modelling: a paradigm that deciphers complex pathological processes".

2007: Drug Discovery Technology Europe, 11th annual conference. 12th-15th March 2007, London, UK. Member of the Scientific Advisory Board. "Discover to Development: predicting safety & efficacy", Session Chair.

2007: Transversale santé. 18th September 2007, Paris. “Analyses intégratives des systèmes complexes et modèles biologiques prédictifs”.
2008: 3d Annual Biomarkers congress. 14th-15th May 2008, Manchester, UK. “Using Systems Biology to Discover Biomarkers in a Neurodegenerative Disease: in Vivo Mechanisms of Creutzfeld-Jakob Pathogenesis and Disease Progression”.
2008: CNS Drug Development. 15th-16th December 2008, London, UK. “Biomarkers in CNS diseases: can serendipity lead to relevance?”, Session Chair.
2008: Edinburgh International Phage Conference. 26th-29th July 2008, Edinburgh, UK. “Engineered phage banks: A functional answer to bacteriological threats”.
2009: 4th Annual Biomarkers congress. 26th -27th February 2009, Manchester UK. “Biological modelling in the discovery of neurodegenerative disease biomarkers”.
2009: Nanotech Conference 2009. 3d-7th May 2009, Houston, USA. “Engineered phage banks: targetable nanodevices as a functional answer to bacteriological threats”.
2009: BE Live IT. 20th-21st October 2009, Brussels, Belgium. “How to maximize synergies between experimental and integrative biology. In-vivo validation of CADI models in Creutzfeldt-Jakob, disease”.
2010: Systems Biology of affective disorders. 6th International Computational Neuropsychiatry Workshop. 7th-8th May 2010, München (Ge). “Pathways of Proteomics in depression - data and modelling”.
2011: Vienna Austria, March 12-15 2011 : 19th European Congress of Psychiatry: “Methodology of Mapping in Integrative Molecular Biology”.
2012: Systems Biology of affective disorders, May 11-12, 2012, München (Ge); F Iris is invited as session chairman to the 8th International Workshop on Computational Neuropsychiatry: Sleep, Affective disorders and Schizophrenia - An integrated view.
2012: Nov. 8-10, Nanjing China; 10th IDDST (International Drug Discovery Science & Technology): “The discovery of Innovative Therapeutics”.
2012: Dec. 7, Pune India; 7th Biocrats conference: “The discovery of innovative therapeutic approaches: Under the street light is not necessarily the right place to search”.
2013: March 24-26 Lyon France: F Iris is invited to contribute to the experts discussions at the 1st "Coordinating Actions Systems-Medicine" stakeholders conference supported by the European Commission during BioVision the world life sciences forum.
2013: Systems Biology of affective disorders, May 3-4, 2013, München (Ge); 9th International Workshop on Computational Neuropsychiatry: Systems Psychiatry of Stress, anxiety and Addiction. “Molecular Pathways of Anxiety”.

<u>10-Year-Track-Record</u>

Over the past 10 years, the activities of Dr Iris have been entirely devoted to two main objectives:
1) The development of novel approaches for heuristic systems biology and their application as effective boosters of R&D in life sciences with both industrial and fundamental applications, and
2) The successful development of BMSystems, a biotech company specialised in systems biology, entirely free from venture capital constrains, capable of serving industrial markets without renouncing to a role in fundamental research through academic collaborations.
In the latter context, the ability to undertake collaborative academic work on a self-financed basis or through specific grant applications was a “sine qua non” condition. Academic laboratories would never be, and have never been asked to pay any fees or services for collaborative work with BMSystems.
Success in all these endeavours is demonstrated by multiple achievements.
- In the domain of industrial activities, BMSystems has an established international track record with the pharmaceutical, the chemical and the cosmetics industries.

- The model of “Alzheimer disease pathogenesis and progression”, constructed in 2007, has now been independently validated (2009-2010) for 75% of its 36 physiological and molecular predictions. Only 5 predictions were demonstrated erroneous and all 5 are associated with a single

mechanism. The remaining 4 predictions are as yet neither confirmed nor infirmed. Hence this model has an advance of at least 3 years over current state of the art.

- The collaborative "Synthon program" (45% financed by the Ministry of Industry) addressed the utilisation of biomass for the production of molecules used as basic building blocks by the chemical industry. To this effect, micro-organisms are utilised as production engines and it becomes necessary to modify their metabolism, and therefore model the modifications required, to achieve production at industrial levels and sustainable costs. One molecule has been produced for L'Oréal (laboratory scale achieved and scaling-up currently underway) and two bacterial strains are under construction for Rhodia and Arkema respectively.

The ability of BMSystems to successfully undertake accurate predictive modelling tasks in a wide variety of complex biological and medical domains, ranging from oncology to cognitive & neurodegenerative diseases, through embryology, therapeutic resistance and microbial metabolism, is a well-established, widely recognised fact that remains without equivalent to date.

- In the domain of fundamental research, by contributing its unique technologies and know-how to carefully selected collaborative programs, BMSystems ensures the medium term maintenance of its scientific acumen (and certainly not its financial survival since such programs require substantial self-financing), while testing the technological developments and forecasting the investments that will be necessary for its future. This is a longstanding policy inherent to BMSystems' industrial development strategy that has been implemented since the creation of the company.

Out of the 5 such fundamental collaborative projects completed to date (2002-2009),

- 4 have led to publications (scientific articles & books chapters),
- 2 have initiated novel drugs development approaches (CNRS & INSERM, published),
- 1 has led to the curtailment of a drug development program that would have resulted in a very costly failure (INSERM, unpublished), and
- 1 has led to the discovery of novel therapeutic mechanisms in CNS dysfunctions ("Class" therapeutics patent) and the development of a new biotech company (TheraNexus).

In this instance, BMSystems holds 30% of the industrial property generated while the academic partner (CEA) holds 70%. In all the other completed projects (4 out of 5), BMSystems did not gain any industrial equity or financial returns but it made significant internal development progresses.

It must be noted that in all the above collaborative fundamental research programs, BMSystems' contributions, while playing key roles in successful completion, were entirely self-financed.

- In the domain of professional excellence, BMSystems has established an international reputation for proficiency, efficacy, reliability and a high capacity to innovate associated with the ability to systematically deliver above and beyond expectations. This is reflected by the induction of Dr Iris into

- The panel of experts on systems biology of the Wellcome Trust (2003-);
- The Evaluation Committee of the funding priorities in the Medical Systems Biology (MedSys) program of the German Federal Ministry of Research (2008-);
- The teaching panel of the COST-Gemini's Training School (Systems Biology Program) of the European Community (2010);
- Numerous invitations to international scientific conferences as invited speaker, session chairman or member of the organizing scientific committee, and
- Work rewarded by a peer-recognized, international industrial award (2009).

In this domain, the emphasis has been placed upon the accumulation of factual achievements as measured by community and business responses and by the ensuing financial health of BMSystems, which rests entirely upon independently corroborated industrial and scientific successes.

- In the domain of innovative technological developments and creation of novel activities, BMSystems has also established a notable international reputation for originality and efficiency.

- In answer to the question "How to detect, in less than three hours, and then efficiently treat infections by an emergent (non-characterised) multi-resistant bacterial pathogen without recourse to vaccines or antibiotics", BMSystems produced three novel technologies (patents WO/2008/093009 [F Iris], WO/2008/093010 [F Iris] and WO/2009/090081 [F Pouillot & F Iris])

allowing 1) to concurrently modify multiple coding regions within a gene while conserving intact any number of coding domains within this same gene, 2) reversibly interrupt the lytic cycle of an obligate virulent bacteriophage (T4) within its host, 3) carry out efficient insertion, by homologous recombination, of any number of engineered genes into the deactivated genomes of a T4 wild-type phage population and 4) reactivate the lytic cycle, leading to the production of engineered infective virulent recombinant progeny. This results in the production of large, genetically engineered banks of lytic viruses containing a very wide spectrum of variants for any chosen phage-associated function, including host-range. Rapid screening of such a bank allows to quickly isolate recombinant particles capable of recognising, infecting and destroying bacteria belonging to species far removed from the original host.

These discoveries led to the creation (2007) of a Bio-Pharma company (Pherecydes Pharma), dedicated to the control of biological threats, entirely financed by two National Defense funds managed by ACE Management (BMSystems owns 40% of this company and the two Defense funds 30% each) and currently in full industrial business development.

- The model describing the mechanisms of pathogenesis and clinical progression of Creutzfeldt-Jakob disease led directly to an understanding of molecular factors playing key roles in the progression and the treatment of psychiatric disorders. This, in turn, led to the discovery of an entirely novel form of treatment for these disabling conditions (tested and validated in vivo) resulting in a joint CEA-BMSystems patent application (WO/2010/029131 A1 [F Mouthon, M Charveriat, J-P Delys & F Iris]) covering a novel therapeutic approach with very wide applications.

Thus, in the space of 10 years, Dr Iris has managed to transform an initial series of significantly limited analytical tools he had invented and contributed to develop into a unique, very efficient and flexible analytical platform allowing to reliably perform multi-scale predictive biological modelling.

The direct consequences have been, in less than 7 years, 1) the invention and patenting of several novel molecular technologies, 2) the discovery and patenting of novel forms of treatment for sociologically & clinically significant neuro-pathologies, 3) the creation of multiple industrially and scientifically successful SMEs (BMSystems being one of them), 4) the development of novel products by established multi-national industrial firms, without 5) ceasing to play an active and recognised role in fundamental research and academic teaching.