

## **Supplementary Material**

### **Anthony William Linnane 1930–2017**

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**Section 1** Honours and Awards (Page 2)

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**Section 3** Supplementary Material to Biographical Memoir (Pages 32–51)

## **1. Honours and Awards - Anthony William Linnane**

- 1972 Fellow of the Australian Academy of Science
- 1973 Lemberg Medallist and Lecturer, Australian Biochemistry
- 1980 Fellow of the Royal Society
- 1990 Honorary Member of the American Society of Biochemistry and Molecular Biology
- 1995 Member of the Order of Australia
- 1996 Emeritus Professor at Monash University
- 1996 Honorary Professor at the University of Melbourne
- 1999 Fellow of the Australian Academy of Technological Sciences and Engineering
- 2000 Distinguished Service Award of International Union of Biochemistry and Molecular Biology
- 2001 Centenary Medal of Australia
- 2005 Honorary Life Member of the Australian Society for Biochemistry and Molecular Biology
- 2007 Honorary Professor at the University of Queensland
- 2013 Adjunct Professor at the University of Sydney

## 2. Publications of Anthony W. Linnane

### Notes:

- (i) Abstracts are not included in this list.
  - (ii) Publications in the series "Biogenesis of mitochondria" are shown with an asterisk. Titles have had the relevant Arabic numeral inserted where this is expressed either as Roman Numeral or included in a footnote in the original publication. Publications in this series do not always appear sequentially in the list below.
1. Eden, E., Harrison, D.D., and Linnane, A.W. (1954). Studies in carbon tetrachloride poisoning. I. The detection and estimation of creatine and related compounds, *Aust J Exp Biol Med Sci* **32**(3), 333-9.
  2. Eden, E., Harrison, D.D., and Linnane, A.W. (1954). Studies in carbon tetrachloride poisoning. II. The effect on creatine metabolism, *Aust J Exp Biol Med Sci* **32**(3), 341-5.
  3. Linnane, A.W., and Still, J.L. (1955). Respiring mitochondria from baker's yeast, *Arch Biochem Biophys* **56**(1), 264-5.
  4. Linnane, A.W., and Still, J.L. (1955). The isolation of respiring mitochondria from baker's yeast, *Arch Biochem Biophys* **59**(2), 383-92.
  5. Linnane, A.W., and Still, J.L. (1955). The intracellular distribution of enzymes in *Serratia marcescens*, *Biochim Biophys Acta* **16**(2), 305-6.
  6. Ziegler, D.M., Linnane, A.W., Green, D.E., Dass, C.M., and Ris, H. (1958). Studies on the electron transport system. XI. Correlation of the morphology and enzymic properties of mitochondrial and sub-mitochondrial particles, *Biochim Biophys Acta* **28**(3), 524-38.
  7. Linnane, A.W., and Ziegler, D.M. (1958). Studies on the mechanism of oxidative phosphorylation. V. The phosphorylating properties of the electron transport particle, *Biochim Biophys Acta* **29**(3), 630-8.
  8. Ziegler, D.M., and Linnane, A.W. (1958). Studies on the electron transport system. XIII. Mitochondrial structure and dehydrogenase activity in isolated mitochondria, *Biochim Biophys Acta* **30**(1), 53-63.
  9. Linnane, A.W. (1958). A soluble component required for oxidative phosphorylation by a sub-mitochondrial particle from beef heart muscle, *Biochim Biophys Acta* **30**(1), 221-2.
  10. Linnane, A.W., and Titchener, E.B. (1960). Studies on the mechanism of oxidative phosphorylation. VI. A factor for coupled oxidation in the electron transport particle, *Biochim Biophys Acta* **39**, 469-78.

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12. Vitols, E., and Linnane, A.W. (1961). Studies on the oxidative metabolism of *Saccharomyces cerevisiae*. II. Morphology and oxidative phosphorylation capacity of mitochondria and derived particles from baker's yeast, *J Biophys Biochem Cytol* **9**, 701-10.
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20. Clark-Walker, G.D., and Linnane, A.W. (1966). In vivo differentiation of yeast cytoplasmic and mitochondrial protein synthesis with antibiotics, *Biochem Biophys Res Commun* **25**(1), 8-13.
21. Huang, M., Biggs, D.R., Clark-Walker, G.D., and Linnane, A.W. (1966). Chloramphenicol inhibition of the formation of particulate mitochondrial enzymes of *Saccharomyces cerevisiae*, *Biochim Biophys Acta* **114**(2), 434-6.
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### 3. Supplementary Material to Biographical Memoir of Anthony William Linnane

#### The diversification years at Monash (1981-1995)

##### *Seeds of change and governance: The Centre for Molecular Biology and Medicine*

As the 1980s commenced, the focus of science and its outcomes began to change for Tony Linnane. He found himself searching more broadly for medical research opportunities, especially those with potential commercial outcomes that could bring in funding not only from the NHMRC but also from corporate and private benefactors and donors.<sup>1</sup> A key change in Tony's personal circumstances in 1980 unexpectedly opened the door to these opportunities. This was Tony's marriage to Daryl Ann Woods in 1980. Daryl's father was Alan Skurrie, a prominent company director, at the time at Amcor. He introduced Tony to the powerful high echelons of the business world of Melbourne. During the mid-1970s Linnane had developed the view that molecular biology was the science of the future, enthusiastically embracing the new technologies of gene analysis and manipulation that could modify the properties of living organisms. He recognised that appropriation of the label "molecular biology" linked to "medicine" could be a winner in the fundraising stakes, and so he founded the Centre for Molecular Biology and Medicine (CMBM) at Monash University in 1983.<sup>2</sup>

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<sup>1</sup> At the outset Tony took the view (rightly or wrongly) that funding for medical research was much more slanted to applicants with medical qualifications. More generally, he felt that there were many aspects of medical research that were "a closed shop to him", so that he had to recruit medically qualified colleagues for collaborative work to "open the door" for him to access clinical material for research and "to get into the medical system", as he saw it. One of Tony's confidants and advisors in this respect was Paul Zimmet, who had carried out his PhD with Joe Bornstein around 1970 and became a distinguished clinician in diabetes research, associated academically with Monash University for almost all of his career. Zimmet introduced Tony to Daryl Woods (née Skurrie).

<sup>2</sup> Linnane was introduced to the roles played by the Club system in the high-end business and legal worlds of Melbourne. He duly took up membership of the Athenaeum Club in Collins Street, where he and his new corporate friends and colleagues would meet, and so set up the Board of Management for the nascent CMBM. The inaugural Board of CMBM was established during 1983 and comprised Sir Brian



The governance structure for CMBM placed itself as a bridge between the academic research world of the university and both the medical and corporate worlds. The university supported the establishment of this novel way to bring in external funds and to expand its activities in modes of translational research. For the next two decades, this worked out very well for Tony Linnane and the CMBM, for which he was the Director for its entire lifetime.<sup>3</sup> Initially the core of the research leadership in CMBM at the Monash Clayton campus was comprised of senior academic staff in the so-called Mitochondria Group of the Department of Biochemistry (Fig. 4 in main text), together with Monash colleagues involved in medical research at other locations.<sup>4</sup> A key person in the development and prospering of CMBM was Michael Kios (Supplementary Fig. 1), who became Tony's right-hand man from 1989, and stayed until the very end.<sup>5</sup> Another very important colleague, who came to CMBM in 1987 was Ian R. Mackay (Supplementary Fig. 2), a distinguished immunologist, who had recently retired at the from the Walter and Eliza Hall Institute for Medical Research, at the University of

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Inglis (Chairman), Charles Trethowan, Bruce Gadsden, Hugh Rogers, John Habersberger and Dennis Corder. CMBM commenced its activities at Monash University in 1984, with the Vice-Chancellor, Professor Raymond (Ray) Martin, joining the Board. Later Board members included Edward (Ned) Churchill, Peter Wade, Jack Seymour, Bill Rogers, Don Hyde, Ed Woods, Glenn Barnes, Abe Monester, Ross Scholes-Robertson, John D'Arcy, John Leach and Royce Abbey (this is not a comprehensive list).<sup>3</sup> Linnane used CMBM at Monash to attract large amounts of external funding in the period 1985-1995, much through the good offices of John Sullivan of Perpetual Trustees. Examples of regular donors included the Baker Trust and the Brockhoff Foundation. From 1993, a fundraising campaign dubbed "The Life and Health Project" secured about more than \$1 million dollars from corporations, high net worth individuals and charitable trusts. An additional very large donation was secured funding from the H&L Hecht Trust for refurbishing the CMBM laboratory/office complex. The Centre had good relations with the Victorian State Government, with senior government leaders attending significant events. CMBM also started receiving Victorian Government infrastructure funding.

<sup>4</sup> Initially, CMBM had "nodes" at the Alfred Hospital and Box Hill Hospital, including the haematology groups of Barry Firkin and Hatem Salem, respectively. Professor Barry Firkin was the first Associate Director of CMBM.

<sup>5</sup> Michael Kios was initially employed in 1982 as technician for Microclinical Chemistry, a small company set up in the Department of Biochemistry by Bornstein and Linnane to run specialised clinical pathology services. He became Resources Manager of CMBM in 1989, when these pathology labs in the department closed. Even after CMBM formally closed its labs at the Epworth Hospital in Richmond in 2008, Kios informally assisted Linnane when the Centre operated out of private home addresses (although Kios had by that time secured other employment).

Melbourne. Mackay provided Linnane with much advice on medical research, occasionally publishing with Linnane, while maintaining his own interests in matters relating to autoimmunity.<sup>6</sup>

Two aspects of Tony's personal life around this time contributed to his reputation as a colourful character. First, was his interest in horse racing, such that on Friday afternoons Tony would take to his office to pore diligently over the form guides for the coming Saturday races and, using a complex predictive system that he had devised, he would work out the best betting strategies for the next day with the assistance of Don Shea.<sup>7</sup> Second, Tony took to smoking small cigars or cigarillos. The departmental folklore of the time was that if you needed to find Tony when he was not in his office, all you had to do was to follow the distinctive aroma to catch up with him!<sup>8</sup>

The various strands of Linnane's scientific work in this period will now be outlined, according to the topic, rather than in strict continuous chronological sequence. Much of this was made possible by Linnane's acquisition of advanced technical equipment for the Department of Biochemistry, for particular use within his research group.<sup>9</sup>

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<sup>6</sup> Mackay was the one of the pioneers of the field of autoimmunity and had been Head of the Clinical Research Unit at WEHI, where he had worked for 24 years until he retired from there in 1987. He moved to Monash shortly thereafter and was joined at CMBM by former WEHI colleagues Senga Whittingham and Merrill Rowley, who carried out laboratory research related to his projects at Monash (including rheumatoid arthritis and diabetes). Mackay became an Honorary Professor of Biochemistry from 1987 until 2000. He was a prolific author and continued to work at Monash on manuscripts, reviews and historical documents until ill health slowed him down in 2017.

<sup>7</sup> Shea (a retired jockey), was hired initially to make the culture media for the yeast research group in the Department of Biochemistry. Later he worked for Microclinical Chemistry as a courier, collecting pathology samples for analysis. Shea retired from Monash in 1986. At one stage, Tony was part of a syndicate that owned a racehorse, trained in the stable of Colin Hayes.

<sup>8</sup> In those days there were no restrictions on smoking in the workplace. When Tony felt heavily under pressure, he would smoke cigarettes. After many years, he eventually gave up smoking completely.

<sup>9</sup> In the departmental and faculty context at Monash, in the early 1980s, Linnane was able to mobilise funding support to secure the installation of a major new equipment facility in Biochemistry in the highest-end protein and DNA technology of the time. With the co-operation of the Applied Biosystems company, who was the innovative leader in this field, the facility was furnished with a protein synthesiser, a protein sequencer and a DNA synthesiser. Linnane hired an experienced chemist, Dr

### *ATP synthase*

Most of this work is described in the main text. One further aspect relating to Linnane's involvement in organisation of conferences on ATP synthase and other topics relating to mitochondria is outlined below.

In the late 1980s, although his direct involvement in research on yeast had virtually ceased, Linnane began to strategically coordinate funding applications with colleagues in the US and Japan to hold specialist international conferences in the East-West Center at the University of Hawaii.<sup>10</sup> The first such conference was held in 1987 on the Molecular, Structure, Function and Assembly of the ATP Synthases.<sup>11</sup> Two later conferences of this type (in 1989 and 1991) focussed more broadly on various aspects of mitochondria, as Tony's interest shifted to the role of mitochondria in ageing.

### *Mitochondria and ageing*

Most of this work is described in the main text. One further aspect relating to the potential role of CoQ in ameliorating bioenergy deficits is outlined below.

A new dimension to the utility of CoQ was brought to Linnane's attention in the early 1990s by his colleague Fred Crane. In addition to its role in mitochondrial OXPHOS,

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Gabrielle L. McMullen, to oversee the facility with support staff provided through departmental and CMBM funding. This was one of the most advanced facilities in Australia at the time and underpinned multiple aspects of Linnane's work after 1980. McMullen was a PhD in Chemistry from Monash, who had recently returned from Freiburg, Germany, after holding a Humboldt Fellowship at the Chemisches Institut. She was also Dean of Mannix College during her tenure of academic positions in Monash Biochemistry 1981-95. She later took up senior academic leadership positions in the Australian Catholic University in Ballarat and Melbourne.

<sup>10</sup> This took a lot of coordination with colleagues in all three countries making separate but coordinated applications to their national funding agencies. Thus, for the first such conference held in 1987, organised by Marzuki, the agencies were in Australia (Department of Science), USA (National Science Foundation) and Japan (Society for the Promotion of Science), with funding facilitated under bilateral US/Australia and US/Japan scientific cooperation agreements, plus additional support from IUB. The proceedings were published as Marzuki (1989).

CoQ was recognised by Crane to be a component of a plasma membrane oxidoreductase (PMOR) enzyme complex. This enzyme complex enabled intracellular NADH to be oxidised to NAD<sup>+</sup>, and could be driven by external electron acceptors such as ferricyanide. Linnane immediately grasped the significance of being able to sustain the metabolic activities of cells with deteriorating OXPHOS capacity in mitochondria, as was thought to be occurring in ageing, by externally providing them with an efficient means of re-oxidising their NADH. Cellular models were set up at Monash using human *rho*<sup>0</sup> cells lacking mtDNA and it was soon shown that they could grow efficiently with either ferricyanide or CoQ added to the growth medium.<sup>12</sup>

This remarkable observation led to studies on animal systems in which functional analyses were carried out on tissues (notably skeletal muscle) from animals that had aged biologically (or in which mitochondrial functions were depleted *in vivo* by treatment with AZT).<sup>13</sup> For this work Linnane collaborated with Anthony (Tony) R. Luff from the Physiology Department at Monash, working with a postgraduate student, Monika Generowicz. The reduction in soleus muscle contractile function caused by AZT treatment of rats was rescued by concurrent CoQ treatment. Likewise, mitochondrial activities in extracts of cardiac muscle from the same rats, functionally depleted by AZT, were also ameliorated by CoQ.<sup>14</sup>

A parallel collaboration with Franklin (Frank) L. Rosenfeldt examined the physiological effects of CoQ on heart function and derived muscle preparations.<sup>15</sup> It was shown that

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<sup>12</sup> Martinus, et al. (1993).

<sup>13</sup> AZT (azidothymidine, also known as zidovudine) was used in therapy for HIV infection. AZT is also an inhibitor of the mitochondrial DNA polymerase, such that cells and tissues in AZT-treated animals have reduced mitochondrial OXPHOS functions.

<sup>14</sup> Linnane, et al. (1995).

<sup>15</sup> Rosenfeldt was a cardiothoracic surgeon at the Alfred Hospital who had research labs at the adjacent Baker Institute in Prahran, Melbourne.

CoQ was very effective in ameliorating age-associated declines in intact rat hearts subjected to pacing and recovery tests; likewise, CoQ rescued the contractile function of human heart muscle preparations (taken as atrial trabeculae, from transplant patients) that were subjected to ischemia and hypoxia.<sup>16</sup> These and other studies showed the potential of CoQ for rescuing the age-associated bioenergy defects in human populations, and Linnane utilised this as leverage to attract much external funding to his research in CMBM.<sup>17</sup>

*Other research at Monash: interferons and cancer mucins*

Two other research topics engaged Linnane's attention in the 1980s and 1990s, primarily because of their potential to spin-off commercialisation opportunities in the medical area. Gary S. Cobon, a former PhD student of Linnane then working on lipids, returned to Monash after postdoctoral work in the laboratory of Wolfgang (Bill) Joklik in Duke University at Raleigh, North Carolina, USA.<sup>18</sup> Cobon had been trained in molecular biology techniques in Joklik's laboratory and had there cloned a gene coding for mouse interferon. Cobon suggested to Linnane to clone human interferon genes and to express interferon in bacteria or yeast. Linnane was able to interest the Commonwealth Serum Laboratories (CSL), through the Director Neville McCarthy, into providing financial support for expressing interferon in yeast. An arrangement was

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<sup>16</sup> Rowland, et al. (1998). Mariani, et al. (2000).

<sup>17</sup> Linnane featured in an ABC *Quantum* program on ageing, entitled "Three Score years and Ten", first televised by the national broadcaster on 2 November 1994. Linnane was filmed taking CoQ tablets each morning and commenting on their effects, as well as visualising laboratory data indicating the beneficial effects of CoQ on bioenergetic functions in tissues with damaged mitochondria.

<sup>18</sup> Joklik was born in Austria in 1926 and moved with his family to Sydney, Australia at age 11. He received his B.Sc. and M.Sc. in biochemistry from the University of Sydney before going on to his PhD at the University of Oxford, UK, which he completed in 1952. He worked at the John Curtin School of Medical Research in Canberra until 1962, then moved to the USA where he established a successful career in molecular virology and public service to the scientific community.

made for one of the personnel at CSL (Ian T. Nisbet) to be seconded to Monash to undertake research towards a PhD under the supervision of Linnane, to be trained in the techniques of interferon gene cloning and gene expression by working at the bench alongside more experienced postdoctoral scientists.<sup>19</sup>

A new human interferon gene was soon cloned at Monash, namely that encoding a protein dubbed IFN-alpha-M1, whose expression in *E. coli* demonstrated a proof of principle.<sup>20</sup> Monoclonal antibodies were made, which recognised members of the human interferon family, in work was led by Paul J. Hertzog.<sup>21</sup> Later work used polyclonal antibodies raised in rabbits against synthetic peptides representing portions of specific interferon species, in work involving Marzuki.<sup>22</sup> All the above studies utilised the Applied Biosystems protein and DNA equipment that Linnane had secured for the Department of Biochemistry.

There then followed a decade of useful contribution to the interferon field, with publications on many aspects including structure-function analysis within the

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<sup>19</sup> These studies on interferon were led in the lab by Manfred Beilharz, with whom Nisbet worked. Work on the yeast expression vector was carried out by Rodney (Rod) J. Devenish, who had carried out his PhD with Lukins and had undertaken postdoctoral work in the USA working on yeast chromosomal biology. He returned to Monash in 1982 with a Vice-Chancellor's fellowship to build such a vector for expression of interferon and other proteins. Devenish also worked with Nagley, applying nuclear gene expression to address mitochondrial research questions.

<sup>20</sup> Linnane, et al. (1984). The funding to CMBM from CSL for interferon production eventually ceased when it became evident that it was cheaper to purchase it than to make interferon in house.

<sup>21</sup> Hertzog obtained his PhD at the University of Melbourne and undertook postdoctoral research on topics related to cancer in the USA (Omaha, Nebraska) and the UK (York). He had organised a conference in the UK on interferon and he had undertaken an EMBO training course on monoclonal antibody production in Basel, Switzerland, under the leadership of Georges J. F. Köhler (who became one of the 3 Nobel Laureates in 1984 honoured for the discovery and production of monoclonal antibodies). Hertzog joined Linnane at Monash in 1982, well qualified for the interferon work. Hertzog separated from Linnane in 1992, moving to the Monash Institute for Reproduction and Development at Monash Medical Centre, where he continued work on interferon and its receptors. He has remained there ever since, while the organisation changed its name to Monash Institute for Medical Research and, most recently, the Hudson Institute of Medical Research, of which Hertzog is Associate Director.

<sup>22</sup> Sattayasai, et al. (1988).

polypeptide backbone, studies of the antiproliferative effects relative to antiviral effects, role of interferons in diseases such as rheumatoid arthritis and multiple sclerosis, and the potential for interferon to be used against melanomas.<sup>23</sup> Several publications on immunity aspects involved Mackay, including the most highly cited of Linnane's interferon publications.<sup>24</sup> Around 1990, attention turned to interferon receptors, initially studied in terms of tissue distribution and specificity, with studies on receptor genes later being carried out.<sup>25</sup> Linnane's last paper on interferon was published in 1995.<sup>26</sup>

The second activity that engaged Linnane was work the development of a diagnostic for bowel cancer, based on mucinous antigens circulating in blood. Associate Professor W.G.R.M. (Bill) de Boer had been characterising such antigens in the human intestine at the Department of Laboratory Medicine, Royal Southern Memorial Hospital, in Caulfield.<sup>27</sup> He had identified two types of antigen, SIMA and LIMA (for small and large intestine mucinous antigen, respectively) using polyclonal antisera obtained by injecting mucin-containing extracts of particular human large bowel cancers into rabbits. Linnane saw the opportunity to prepare monoclonal antibodies using the hybridoma facility that Hertzog has set up in his group in relation to interferon research (see above), which could provide much more incisive detail of normal and aberrant mucin production in both development and cancer.

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<sup>23</sup> Some of this work was carried out in collaboration with Paula Pitha-Rowe (Johns Hopkins University, Baltimore, USA) (Beilharz, et al. (1988).

<sup>24</sup> Johns, et al. (1992). This ranks 20th in Linnane's publications overall.

<sup>25</sup> Payne, et al. (1994).

<sup>26</sup> Ralph, et al. (1995).

<sup>27</sup> De Boer had previously been at the Monash Department of Pathology, based at the Alfred Hospital, and had worked with Richard C. Nairn (Foundation Professor of Pathology) on immunohistological studies of human tumours, using fluorescently labelled antisera.

Following the successful production of such monoclonal antibodies in 1987 there was a recognition that a new reliable diagnostic might indeed be achievable, particularly with SIMA.<sup>28</sup> Patent protection for the diagnostic potential of these newly isolated monoclonal antibodies together with funding for commercial development was soon obtained. A company Mucan Pty Ltd was established with the participation of Bruce Gadsden, one of the early members of the CMBM Board of Management. Subsequent work described the expression and location of these SIMA and LIMA antigens in normal and cancerous conditions and led to a deeper understanding of the nature of the mucins themselves. These studies showed that SIMA and LIMA are oncofoetal antigens, in that they are expressed normally in embryonic development but not in normal adult tissues; expression resumes, however, in many gastrointestinal cancers. The final two of several publications on mucinous antigens over the period 1991-6 described the characterisation of a particular monoclonal antibody 4D3 detecting the SIMA glycoprotein in the serum of patients with colorectal cancer, and the characterisation of the tumour-associated carbohydrate epitope recognised by that monoclonal antibody.<sup>29</sup> However, in trials carried out in Japan at Eisai Co. Ltd., a major pharmaceutical company, while the Monash monoclonals gave a good signal in serum for a substantial proportion of known cancer patients, there were too many false negatives. Even when a further antibody recognising CEA (carcinoembryonic antigen) was applied in concert with 4D3 to improve coverage of positives, the data were not enough to convince Eisai (nor any other investor or pharmaceutical company) to continue to support the Monash mucin antibody work, which thus eventually lapsed.

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<sup>28</sup> Hertzog, P.J., et al. (1987).

<sup>29</sup> Pinczower, et al. (1993). Pinczower, et al. (1996).



### **The post-Monash years (1996-2017)**

As part of the separation from Monash, financial arrangements were made for CMBM to be reimbursed funds from a large private grant that had already been spent on the refurbishment of Centre laboratories at Monash, officially opened in 1995 by the Premier of Victoria, the Hon Jeffery Kennett. The Centre moved initially into temporary accommodation at the Repatriation Hospital site in Heidelberg, while a more permanent home at the Epworth Hospital in Richmond was under construction. When Linnane moved from Monash in 1996 CMBM had just 6 staff, but this number grew to reach 35 in the ensuing few years as the Centre grew. The new Epworth facilities for CMBM on the corner of Hoddle Street and Bridge Road in Richmond were officially opened in October 1997 by the Victorian Minister for Health, the Hon. Rob Knowles.

Research continued in the relocated CMBM on the ageing and bioenergy insufficiency projects, which led to several publications from solely within CMBM and more from continuing collaborations with researchers still at Monash and elsewhere. In 1997, Linnane secured a very large grant from the Australian Tea Tree Oil Research Institute (ATTORI) based on Northern NSW. The goal was to develop a bioenergy diagnostic in order to determine an individual's profile to assist in the treatment of bioenergetic decline (using CoQ with additional supplements including uridine). This idea was an early form of the present-day notions of personalised or precision medicine. The funding from ATTORI enabled CMBM to be equipped with a full array of modern research equipment. Linnane hired many new research staff, including some who had been PhD students at Monash in his mitochondria team many years before. However, the proposed diagnostic for the state of ageing in individual human subjects never eventuated. Despite some promising early clinical trials on that and other projects with

commercial potential, the budget of CMBM became increasingly strained, leading to staff losses and curtailment of the laboratory research activities. CMBM closed its doors at the Epworth in 2008.

Linnane's publications after 2002 were, for the most part, theoretical or review articles on his ideas on bioenergetic remediation and the possible biochemical factors involved. Many of these were co-authored with Luis Vitetta (Supplementary Fig. 3), a specialist in biopharmaceuticals and aspects of complementary medicine, with whom Linnane maintained a close working relationship for twenty years.<sup>30</sup> Linnane's first contact with Vitetta was when the latter was at Swinburne University in Melbourne (in the Graduate School of Integrative Medicine, working with Avni Sali). Coincident with Vitetta's later move to Brisbane, Linnane was appointed an Honorary Professor at the University of Queensland in 2007 to perform consultative work with Vitetta at the Princess Alexandra Hospital in Brisbane. In Brisbane, Linnane met Peter Brooks (then Dean of Medicine at the University of Queensland) who assisted Linnane both there and after Brooks' own retirement in 2009 when he moved to Melbourne.<sup>31</sup> After Vitetta moved to Sydney in 2013 as Director of Medical Research at MedLab Clinical Ltd, both he and Linnane became adjunct Professors in the School of Medicine at the University of Sydney from 2014. Linnane still lived in Melbourne and was involved in clinical trials both in Sydney and in Melbourne, almost to the day of his passing.

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<sup>30</sup> Luis Vitetta was a medical graduate in Melbourne who was working in palliative care when he met Linnane at the Repatriation Hospital in 1997. He was at Swinburne from 1999-2005, then spent a year with Linnane at CMBM (Epworth) before moving to the University of Queensland from 2007-13 at the Centre for Integrative Clinical and Molecular Medicine. He moved to Sydney in 2013 to become Director of Medical Research at MedLab Clinical Ltd.

<sup>31</sup> Brooks made arrangements with Linnane and Vitetta for the by now superfluous equipment at CMBM to be purchased for use at the University of Queensland.

## **Contributions to societies and international organisations**

### *Australian Academy of Science*

After his election to the Australian Academy of Science in 1972, Linnane served on several National Committees and was Chair of the Victorian Regional Group from 1982-1983. After a gap of three decades, Tony renewed his engagement with the Victorian Regional Group and also participated in mentoring young scientists.

### *ABS/ASBMB*

Tony Linnane made many contributions to the Australian Biochemical Society (ABS), which was founded in 1955 and was the forerunner to the Australian Society for Biochemistry and Molecular Biology (ASBMB).<sup>32</sup> Tony first became involved in ABS in Sydney, leading to his becoming the NSW State Representative 1959-1960, then Secretary 1961-1966 (moving to Monash in 1962). Linnane's main contribution as Secretary was to ensure an international presence at the annual ABS conferences through the bringing of at least one eminent international speaker, who would not only participate in the conference (Supplementary Fig. 4) but who would also visit other locations in Australia.<sup>33</sup>

Linnane was awarded the Lemberg Medal of ABS in 1973, which is the premier award for research contributions by a member of ABS. He was President of ABS 1974-1976 (serving as President-Elect in 1973 and Past-President in 1977). He was made an

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<sup>32</sup> The events leading up to the foundation of ABS in 1955, as an outgrowth of ANZAAS Section N, are briefly recounted by Friedman (2010).

<sup>33</sup> In the 1980s, when airfares had become cheaper, the practice evolved within ABS to have a larger number of international speakers at each annual conference of the society. The international speakers were no longer obligated to visit other locations in Australia (although some did, of course, because of their own connections to local colleagues).

Honorary member of ASBMB in 2005 in recognition of his contributions to the Society (which had changed its name in 1990).<sup>34</sup> Linnane and many other previous Presidents of ABS/ASBMB gathered in Adelaide in 2005 as part of the Golden Jubilee celebrations of the society (Supplementary Fig. 5).

As President of ABS, Tony worked hard to bring the first IUB Congress to the Southern Hemisphere, and his efforts resulted in the 12th IUB Congress being held in Perth WA, in 1982.<sup>35</sup> This Congress brought many distinguished biochemists to Australia that year and was a great scientific success, although the Congress was not without budgetary problems.<sup>36</sup> Many prominent visiting speakers also participated in satellite meetings.<sup>37</sup>

The Congress and IUB business activities were unfortunately affected by political aspects (external to Linnane but causing him much frustration) that resulted in denial by the Australian Government of entry visas to one of the Russian delegates.<sup>38</sup> This led to somewhat bizarre complications for the 11th Ordinary General Assembly of IUB, in

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<sup>34</sup> Friedman (2010).

<sup>35</sup> There is a 6-year lead-up to any Congress of IUB/IUBMB. Thus in 1976, Linnane as President of ABS with Bill Elliot as Past President of ABS went to the IUBMB Congress in Hamburg, Germany, to present to the IUB General Assembly the invitation to hold the Congress in Australia in 1982.

<sup>36</sup> The attendance of paying registered participants was not as numerous as hoped, because of the location in Perth, WA, which at the time was expensive to travel to from the Eastern States of Australia and also not a well-known destination from travellers from the US and Europe. This was one of the factors that caused budgetary issues between the Conference Organising Committee, led by Linnane, and the Australian Academy of Science, which underwrote the IUB Congress in Perth.

<sup>37</sup> These included the International Conference on Manipulation and Expression of Genes in Eukaryotes held at Monash University, during the week prior to the Congress (Nagley et al., 1983). Two other satellite meetings were held during that same week on the Indian Pacific train from Sydney to Perth over 3-4 days!

<sup>38</sup> The issue for the Government of the day, led by the Hon. Malcolm Fraser, was that the head of the delegation to IUB from the Soviet Union, Professor Yuri Ovchinnikov, was not only vice president of the Soviet Academy of Sciences but also a member of the Central Committee of the Communist Party of the Soviet Union. Ironically, Ovchinnikov had been in Australia as a visiting lecturer not long before the Congress, but now, as the head of the Russian delegation to the IUB Congress, he was regarded as a political person. Urgent pleas from both Congress Organisers and IUB to the Australian Government were to no avail; the decision to deny his visa was not rescinded, with the result that the entire delegation did not attend.

which resolutions were voted by the delegates present in Perth (Part 1). To allow the Russian delegates to record their votes, Part 2 of the General Assembly took place 3 weeks later in Moscow (all this was ably managed by Bill Whelan, then IUB General Secretary).

#### *FAOB/FAOBMB and IUB/IUBMB*

Tony became involved in regional as well as international organisations.<sup>39</sup> Such involvement was encouraged by various Presidents of IUB/IUBMB, especially E.C. (Bill) Slater (Netherlands, 1988-1991) and Kunio Yagi (Japan, 1994-1997). Tony greatly valued these friendships and these individuals, together with Brian F.C. Clark (Denmark, IUBMB President 2000-2003), had much influence on his professional and research life.<sup>40</sup> With the formation of the Federation of Asian and Oceanian Biochemists (FAOB) in 1972, pressure from IUB colleagues was placed on Tony to become the foundation president, but this did not eventuate; that role was filled by Edwin C. Webb from Queensland, Australia.<sup>41</sup> Linnane did eventually become President of FAOB during 1975-1977. He was instrumental with Kunio Yagi in the establishment of triennial Congresses of FAOB (on a similar cycle to those of IUB, but one year out of phase) with the first such FAOB Congress being held in Nagoya, Japan in 1977, which was a very successful event.<sup>42</sup> The pattern then followed of an annual

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<sup>39</sup> Histories of the development and organisation of IUB/IUBMB and FAOB/FAOBMB, up to 2005 and 2006, respectively, have been published (Slater, 2005; Svasti and Sawyer, 2006).

<sup>40</sup> Linnane (2010).

<sup>41</sup> E.C. Webb was a highly accomplished enzymologist. Together with Malcom Dixon he was author of the comprehensive treatise entitled *Enzymes* (appearing in several editions from 1958 to 1979), indispensable to many biochemists of that period.

<sup>42</sup> Linnane (1978). The Congresses of FAOB (becoming FAOBMB in 1994) were originally held in the year following that of the IUB/IUBMB Congress, so as not to clash. However, from 2003 onwards (for complex reasons) the FAOBMB Congresses were then held in the same year as that of the IUBMB Congress. Nowadays, when the IUBMB Congress is held in the FAOBMB region, the Congresses are combined into a single event for that year.

Symposium of FAOB, each time in a different country, until the next FAOB Congress. [Note that after IUB changed its name to IUBMB in 1991, FAOB became FAOBMB in 1993].

When Linnane became Treasurer of IUB for 9 years between 1988 to 1997, he was a very thorough administrator and established a firm basis for managing the growing IUB funds (which were accruing largely through its activities in publications). He was a driving force for the IUBMB Conferences held in each of the two intervening years between the triennial IUBMB Congresses (as had been the practice in the regional biochemical community of FAOB, mentioned above). These IUBMB Conferences took place during the period 1992 to 2016, the first being held in Nagoya, Japan and the last in Vancouver, Canada.<sup>43</sup>

During the late 1970s Linnane worked with the leadership of IUB to start a new journal specialising in rapid publication of short reports. He became founding Editor of *Biochemistry International*, whose quality increased over time but remained in the middle-rank in its field. The name of the journal was changed to *Biochemistry and Molecular Biology International* (BAMBI) in 1993. After Linnane left the position of Editor in Chief in 1998, the journal eventually morphed into *IUBMB Life*.<sup>44</sup>

For his contributions to the international biochemistry and molecular biology communities, Linnane was awarded the IUBMB Distinguished Service Award in 2000.

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<sup>43</sup> After 2016, IUBMB Focused Meetings were introduced, about 3 per year, on specialised topics and at a smaller scale than the more generalised IUBMB Conferences of the previous 25-year period.

<sup>44</sup> After 1998, under the IUBMB presidency of Bill Whelan, the editorship of BAMBI for a short time was taken over by Kelvin J.A. Davies (University of Southern California, USA). The name of the journal was changed in 1999 to *IUBMB Life*, published by Taylor and Francis Journals Inc. Not long after, the editorship changed to Bill Whelan (University of Miami, FL, USA) and Angelo Azzi (University of Bern, Switzerland and later Tufts University, Boston MA, USA); both are Past-Presidents of IUBMB. The publishers of *IUBMB Life* later became John Wiley & Sons Inc.

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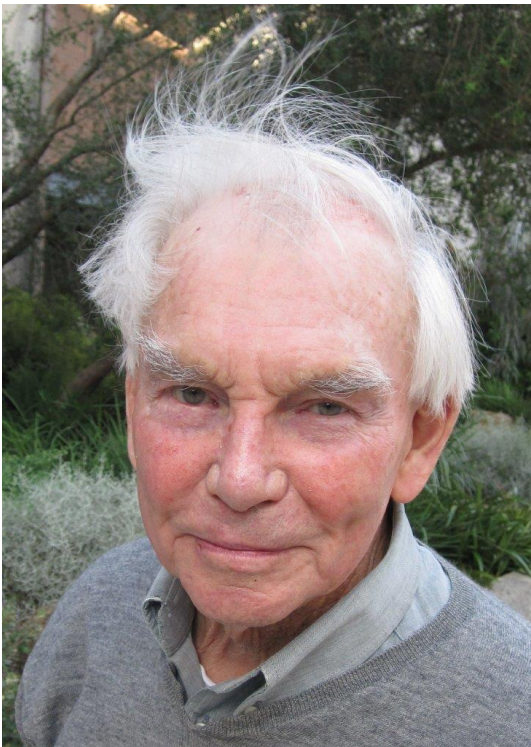
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## Supplementary Figures



**Supplementary Figure 1.** Michael Kios, in 2018 (image taken by the author).



**Supplementary Figure 2.** Ian R. Mackay, in 2011 (image taken by the author).



**Supplementary Figure 3.** Luis Vitetta (*left*) in deep conversation with Tony Linnane, in Melbourne, 2015 (image courtesy of Luis Vitetta).



**Supplementary Figure 4.** Taking a tea break at ABS Conference in Brisbane, 1966.

*From left:* J.E. O'Hagen, F. Gordon Lennox, Joe Bornstein, Tony Linnane (ASBMB Archives).



**Supplementary Figure 5.** Fifteen ABS/ASBMB Presidents gathered at the ComBio2005 gala dinner in honour of the Society's Golden Jubilee celebrations, held in Adelaide.

*Back row (from left):* Denis Crane (2007–2008), Nick Hoogenraad (1997–1998), Philip Kuchel (1994–1996), Gerry Wake (1984–1986), John Ballard (1982–1984), John Wallace (2003–2004), Geoffrey Kellerman (1980–1982), Keith Boardman (1976–1978), Tony Linnane (1974–1976), Bill Elliott (1972–1974).

*Front row (from left):* Bruce Stone (1988–1990), Frank Gibson (1978–1980), Phillip Nagley (2005–2006), John de Jersey (2001–2002), Bill Sawyer (1990–1992)  
(ASBMB Archives).