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Epigenetic therapy (medicine in the bottle) has the potential to stop the outgrowth of endocrine resistant estrogen receptor positive (ER+) breast cancer cells by remodelling the 3D cancer epigenome to suppress the ER+ resistant cell growth (the noxious weed that can overtake and kill the rest of the plants in the garden). AI-generated image in DALL·E3 and manually edited in Procreate and Adobe Photoshop. Image courtesy of Christopher Molloy (Chris O'Brien Life House) and Elyssa Campbell, Jo Achinger-Kawecka and Sue Clark (Garvan Institute of Medical Research).

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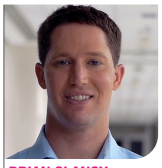

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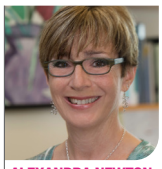

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A Role for RNA in Stabilising Chromatin at Repressed Genes

Healy E#, Zhang Q#, Gail EH, Agius SC, Sun G, Bullen M, Pandey V, Das PP, Polo JM, Davidovich C*. The apparent loss of PRC2 chromatin occupancy as an artifact of RNA depletion. *Cell Rep* 2024;43(3):113858.
#Contributed equally to this work
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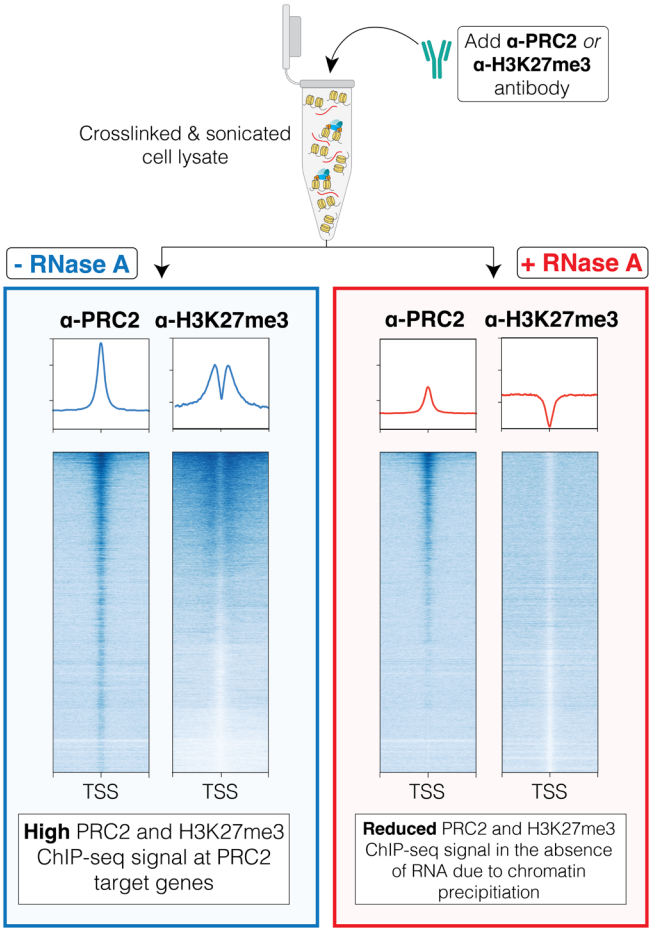
Much of the mammalian genome is transcribed with many of these RNAs being retained in the nucleus. This nuclear RNA has been proposed to serve an architectural role in chromatin organisation with its depletion leading to disruption of both active and repressed chromatin domains. RNA physically binds many chromatin modifiers, with the H3K27me3 methyltransferase polycomb repressive complex 2 (PRC2) among the most studied in this context. The enzymatic activity and localisation of PRC2 are critical for the repression of cell type-specific genes and often perturbed in disease. A functional role for PRC2-RNA interactions has been intensely debated, with seemingly opposing models proposed, such as RNA-mediated recruitment of PRC2 or antagonistic interactions. At present, there is ambiguity in the field on how – and to what extent – RNA regulates the chromatin occupancy and enzymatic activity of PRC2.

RNase treatment of chromatin is a common perturbation experiment that has been used recently to ascribe functional roles for RNA in the regulation of PRC2. Accordingly, the treatment of chromatin with RNase A during immunoprecipitation (termed rChIP-seq) led to the depletion of PRC2 subunits from chromatin, which suggested a functional role for PRC2-RNA interactions. Data generated with this rChIP-seq method was used to support a model where RNA is required for PRC2 chromatin occupancy through an 'RNA bridge'. In our study, we confirmed that RNase A treatment during chromatin immunoprecipitation indeed reduces PRC2 chromatin occupancy. However, to further challenge this rChIP-seq assay, we assayed the H3K27me3 histone modification as a control. H3K27me3 was chosen as we had no reason to assume that an RNA bridge would be present between H3K27me3 and chromatin. Unexpectedly, the RNA-dependent reduction in PRC2 occupancy that was observed by rChIP-seq was also accompanied by a concurrent loss in H3K27me3 signals.



To perform rChIP seq, human iPS cells are crosslinked, lysed and sonicated, then incubated with antibodies against PRC2 subunits or the histone modification H3K27me3, either in the presence or absence of RNase A. When RNA is degraded the rChIP-seq signal signal both PRC2 and H3K27me3 is artificaily reduced due to precipitation of nontargeted DNA which is sequenced at the expense of DNA from targeted regions. This occurs despite the factors in question – PRC2 and H3K27me3 – remaining on chromatin.

There was no obvious biological explanation for the loss of H3K27me3 after RNA depletion, as RNase treatment was carried out after chromatin was crosslinked and isolated from cells, and hence cannot be due to the loss of PRC2 methyltransferase activity. To help explain this phenomenon, instead of proceeding directly to Next Generation Sequencing after the rChIP assay, we performed ChIP followed by quantitative PCR (rChIP-qPCR). Importantly, ChIP-qPCR can directly quantify the immunoprecipitated sample with respect to the input, without reliance on genome-wide normalisation effects. Strikingly, we found that RNase A treatment led to the increase of both PRC2 and H3K27me3 ChIP-qPCR signals. This was in direct disagreement with the ChIP-seq results we obtained with RNase A treatment, where RNase A treatment seemingly depleted H3K27me3. We tracked this observation to a global gain of non-targeted chromatin, which led to excess DNA from non-targeted genomic regions. This non-targeted DNA is then sequenced at the expense of DNA from facultative heterochromatin, resulting in the artificial loss of ChIP signals despite the factors in question – PRC2 and H3K27me3 – remaining on chromatin.

Based on this data we found no evidence for the existence of an 'RNA bridge' between PRC2 and chromatin. Our results imply that the RNA bridge model has been supported based on an experimental artifact. More positively, our results suggest a crucial role for RNA in solubilising chromatin which should be considered when developing new experimental approaches in this area. Collectively, our results point to substantial technical limitations with the usage of RNase treatment of chromatin during ChIP, but also imply broader roles for RNA in stabilising chromatin structure, beyond direct interactions with chromatin modifiers.

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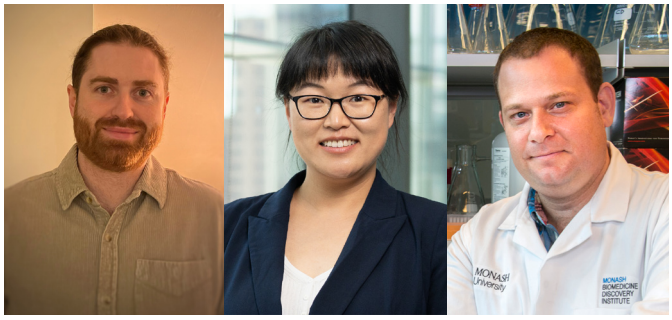

From left: Evan Healy, Qi Zhang and Chen Davidovich.

Boosting Chaperones Early Protects the Brain From TDP-43-Mediated Neurodegeneration

San Gil R, Pascovici D, Venturato J, Brown-Wright H, Mehta P, Madrid San Martin L, Wu J, Luan W, Chui YK, Bademosi AT, Swaminathan S, Naidoo S, Berning BA, Wright AL, Keating SS, Curtis MA, Faull RLM, Lee JD, Ngo ST, Lee A, Morsch M, Chung RS, Scotter E, Lisowski L, Mirzaei M, Walker AK*. A transient protein folding response targets aggregation in the early phase of TDP-43-mediated neurodegeneration. *Nat Commun* 2024;15(1):1508.
***Corresponding author: adam.walker@uq.edu.au**

The process of protein aggregation is strongly associated with the death of neurons in neurodegenerative diseases. Aggregation and cytoplasmic accumulation of normally nuclear TAR DNA-binding protein 43 (TDP-43) is increasingly associated with a wide range of these neurodegenerative diseases, including motor neuron disease (MND)/amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD) and Alzheimer's disease. The misfolding of TDP-43 that leads to its aggregation and inclusion formation in the cytoplasm of neurons is likely a process that occurs over decades in TDP-43-mediated disease. One of the questions in the field is what are the early molecular consequences of TDP-43 aggregation that contribute to neurodegeneration. Hampering progress in addressing this has been the inability to access brain tissue of individuals with TDP-43-mediated disease over time and a dearth of preclinical mouse models that recapitulate the key molecular pathologies (namely cytoplasmic TDP-43 protein aggregation and neurodegeneration).

Developed nearly ten years ago, the rNLS8 TDP-43 mouse model has become one of the gold standard models in the field, developing an MND-like disease phenotype and TDP-43 pathology, and has been adopted for both mechanistic and drug development studies in academia and industry in many countries. To understand the biochemical alterations occurring throughout TDP-43-mediated disease, we therefore developed a global unbiased map of the proteomic signatures in the rNLS8 mouse cortex prior to and at

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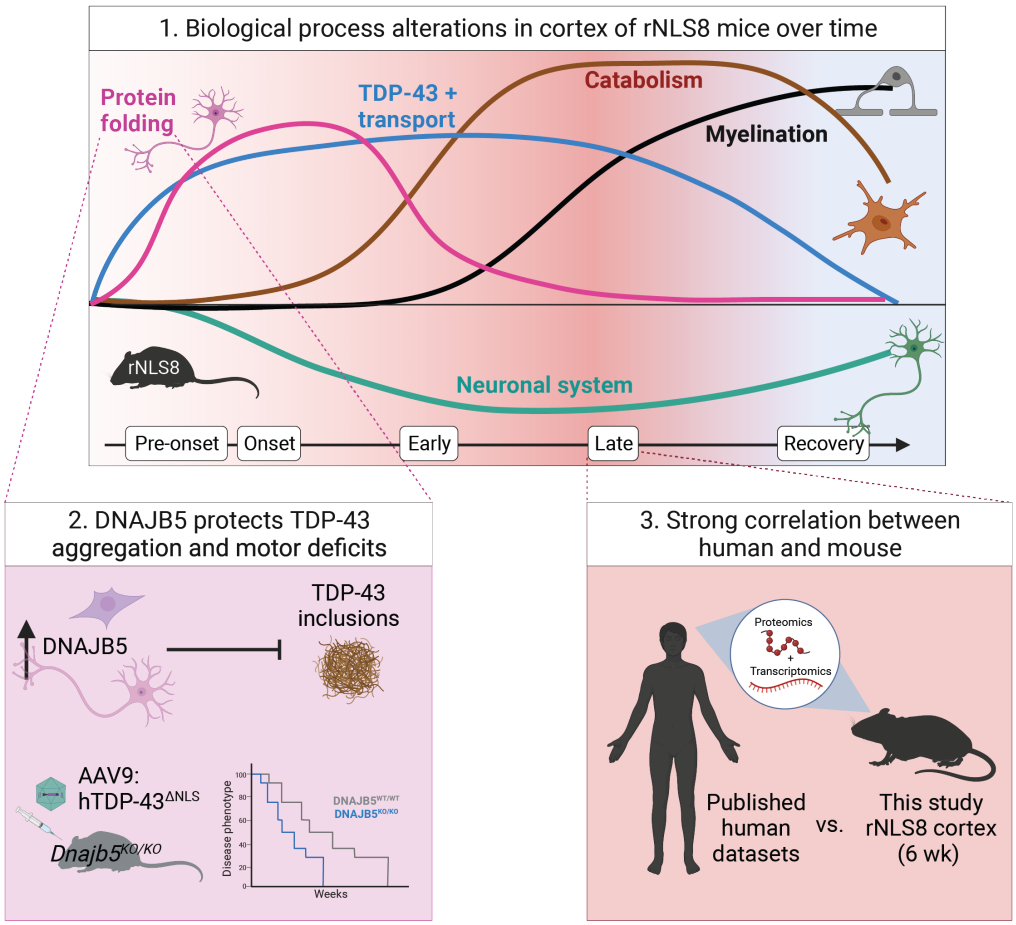

(1) A schematic of the alterations to biological processes in the rNLS8 cortex over the time course of disease identified by quantitative proteomics. Increases in the abundance of protein folding factors define early disease.
(2) DNAJB5 protects against TDP-43 aggregation and motor deficits.
(3) A strong correlation in the proteomic signature of late disease mouse and post-mortem cortex tissue of cases with TDP-43 proteinopathy validate the rNLS8 mouse model.
Figure from Nat Commun *2024;15(1):1508 (CC-BY 4.0 license).*

onset, early and late stages of disease. In the interest of ensuring that the longitudinal proteomic dataset was open-access and user-friendly, we developed a complementary webtool called 'TDP-map', allowing simple interrogation of the full dataset for researchers' favourite proteins of interest: https://shiny.rcc.uq.edu.au/TDP-map/

We found that neuronal-specific expression of cytoplasmic TDP-43 triggered a maelstrom of neuronal and glial disease processes, which changed over the disease course. Amongst these, we identified distinct subsets of proteins that showed different correlated patterns of abundance over time. Gene ontology analysis also revealed that each subset was enriched for distinct biological pathways. For example, one subset showed an increase in abundance of proteins that were enriched for protein folding factors prior to onset and at the earliest stages of disease, but we found that this response was not sustained at later disease timepoints (magenta line in **Fig 1**). Seven of the proteins are members of a protein–protein interaction network, suggesting a coordinated function in disease, namely, HSP 90 alpha family class B member 1 (HSP90AB1), HSP90 co-chaperone cell division cycle 37 (CDC37), DnaJ homolog subfamily B member 5 (DNAJB5), calreticulin (CALR), stress-induced phosphoprotein 1 (STIP1), translocase of outer mitochondrial membrane 34 (TOMM34), and cytoplasmic dynein 1 intermediate chain 2 (DYNC1i2). Since protein folding factors such as anti-aggregation protein chaperones could potentially protect against TDP-43 aggregation, we focused our attention on this group.

We followed up on Dnaj homolog subfamily B member 5 (DNAJB5; a J-domain protein family member) because it showed the highest fold increase and colocalised with TDP-43 inclusions in the cortex of rNLS8 mice as well as in the motor cortex of people who had died with MND with or without frontotemporal dementia. DNAJB5 overexpression decreased TDP-43 aggregation in cell and cortical neuron cultures, and knockout of *Dnajb5* exacerbated TDP-43 aggregation in cells and worsened motor impairments caused by AAV-mediated

cytoplasmic TDP-43 expression in mice. These data provide strong evidence to support the importance of DNAJB5 as a key protective factor in cortex neurons against the onset of cytoplasmic TDP-43-associated motor impairments, particularly in early disease.

Together, these findings reveal that onset, early, and late disease timepoints have distinct biochemical signatures that represent both protective and deleterious pathways in neurodegeneration. Findings at early disease timepoints in the rNLS8 cortex may accelerate our understanding of the mechanisms driving disease progression and reveal key targets with future therapeutic potential. Modulation of TDP-43 aggregation by targeting protein folding factors discovered in this study is a promising therapeutic strategy to treat TDP-43 proteinopathies with the goal of helping people living with these diseases live longer, better lives.

Adam Walker (left) and Rebecca San Gil.

Rebecca San Gil and Adam Walker
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HIV Capsid's Solo Act: Navigating the Nuclear Pore Complex

Dickson CF, Hertel S, Tuckwell AJ, Li N, Al-Izzi SC, Ariotti N, Sierecki E, Gambin Y, Morris RG, Towers GJ, Böcking T, Jacques DA*. The HIV capsid mimics karyopherin engagement of the FG-nucleoporins. *Nature* 2024;626:836–842.
***Corresponding author: d.jacques@unsw.edu.au**

HIV is a retrovirus. This means that it has to complete two processes in order to infect a cell. Firstly, it must convert its single-stranded RNA into double-stranded DNA (reverse transcription); then it must incorporate this DNA into host chromatin (integration). Accessing host chromatin is one of the challenges that all retroviruses must overcome. While most achieve this during mitosis when the nuclear envelope dissolves, HIV is able to infect non-dividing cells. How it breaches the nuclear envelope was a long outstanding question in HIV biology.

The doorway to the nucleus is the nuclear pore complex (NPC). Comprised of over 1,000 individual nucleoporin (Nup) proteins, it is one of the most complex macromolecular assemblies known. Crucially, the NPC is a mix of structured scaffolding domains and unstructured domains anchored in the nuclear envelope. The unstructured domains are enriched in phenylalanine–glycine (FG) dipeptide motifs and project into the central transport channel of the NPC. The hydrophobic phenylalanine sidechains cause these unstructured domains to adhere to each other, and they form phase separated condensates *in vitro*. By establishing a separate phase in the central transport channel, the NPC effectively separates the nucleus from the cytoplasm with an aqueous barrier that can only be crossed by macromolecules that are soluble in this phase.

The karyopherins are cellular proteins that chaperone cargoes across NPC. They achieve this feat by having multiple, weakly-interacting FG-binding sites on their surface. This property allows them to partition into the FG-containing phases.

Previous work by us and others had shown that the HIV capsid makes direct interactions with a number of host proteins in the early stages of infection. Crystal structures of three of these proteins (SEC24C, Nup153 and CPSF6) had been solved in complex with the HIV capsid protein. Each of these host proteins is bound via a linear peptide motif with overlapping footprints on the capsid surface. While adopting different spatial arrangements, these three proteins all buried a conformationally-identical FG-motif in a conserved pocket on the capsid.

As one of these cofactors was a Nup protein and individual NPCs carry over 5,000 FG-motifs, we reasoned that perhaps there were more interactions to be found. The challenge was that Nup proteins tend to be essential for cell viability, making them recalcitrant to depletion and manipulation *in cellulo*. To overcome this, we developed a method to dissect the NPC *in vitro* by expressing individual Nups fused to GFP in a cell-free system. We then added fluorescent capsid assemblies and observed the interaction by fluorescence fluctuation spectroscopy. Using this approach, we identified that each of the FG-repeat Nups bound to the HIV capsid (**Fig D**), that the interaction was specific to the FG-repeat domains, and

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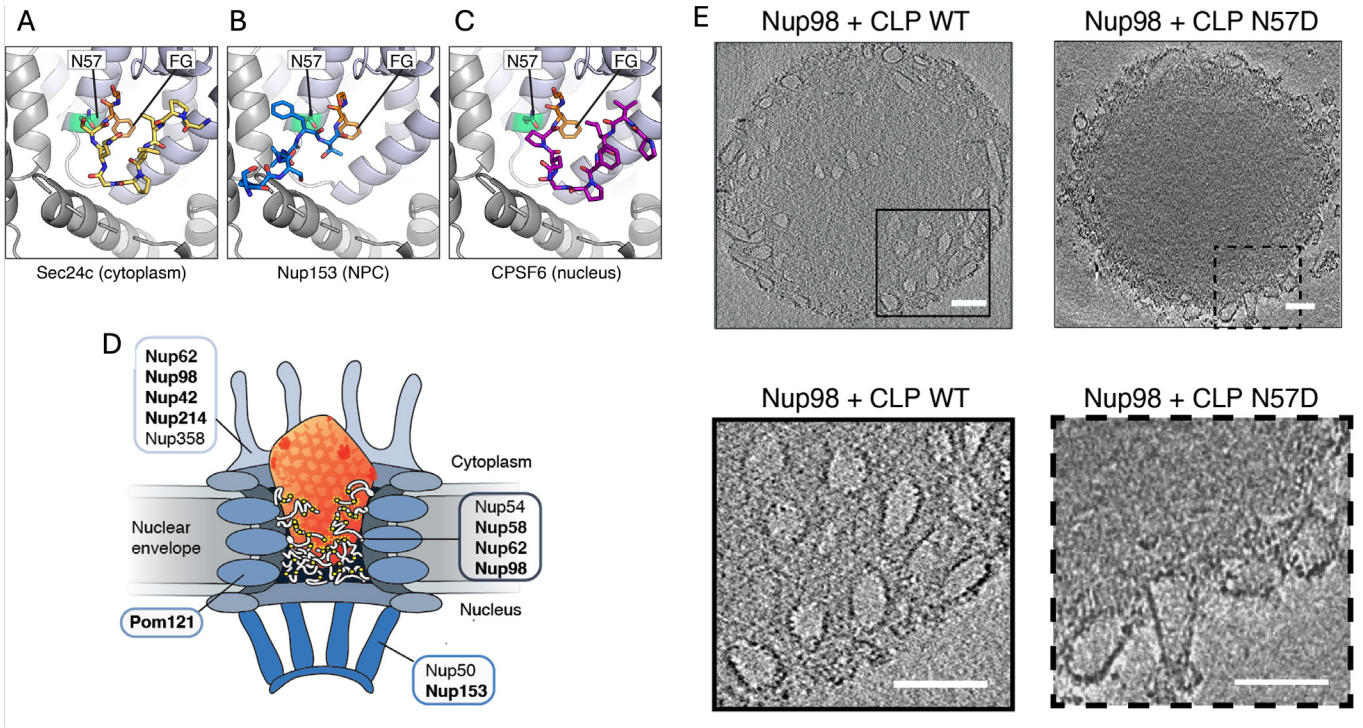

*Crystal structures of HIV capsid bound to (**A**) Sec24C, (**B**) Nup153 and (**C**) CSPF6. FG-motif is shown in orange. (**D**) the HIV capsid interacts with the FG-Nups found within the central transport channel of the NPC. (**E**) Assembled capsid-like particles can penetrate Nup98 condensates* in vitro*, but are excluded upon mutation of the FG-binding site (N57D).*

that the interaction was driven by avidity. Furthermore, by using specific mutations on the HIV capsid surface, we could localise the interaction to the FG-binding pocket observed in the previous crystal structures.

While this method confirmed that the capsid protein and FG-Nups could interact, it did not explain how the assembled capsid (which typically comprises approximately 1,200 copies of the capsid protein with a molecular weight of about 28 MDa) could penetrate a barrier that usually excludes molecules one thousandth the size. To answer this question, we made mCherry-fusions of the capsid protein, assembled capsid-like particles and added them to phase-separated Nup98 *in vitro*. Under these conditions, mCherry is excluded from the Nup98 droplets. However, the fusion to the HIV capsid protein enabled these constructs to enter these FG-containing phases. Furthermore, we could see the assembled lattices penetrating spherical FG-phases by cryoEM. All of these properties were lost upon mutation of the FG-binding site of the capsid (**Fig E**).

Our study provides a new physicochemical model for how viruses, and indeed other large cargoes, can overcome the nuclear pore complex and therefore non-destructively breach the nuclear envelope to gain access to cellular DNA.

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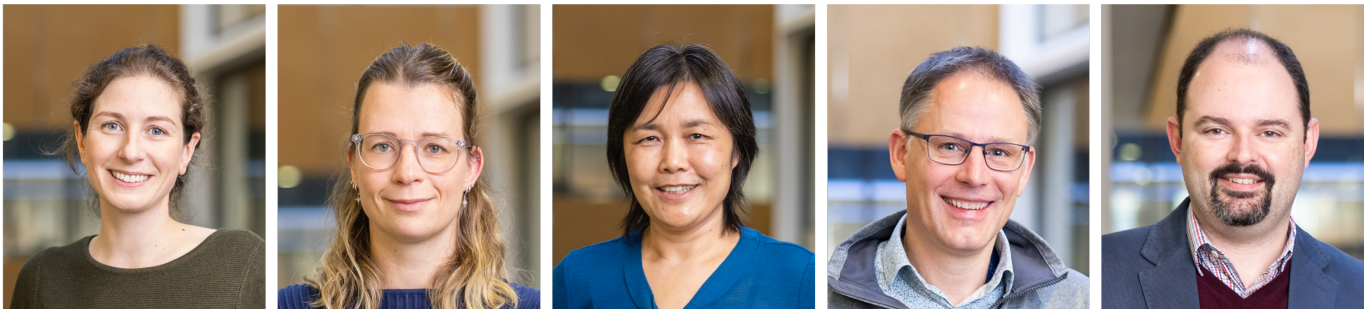

From left: Claire Dickson, Sophie Hertel, Nan Li, Till Böcking and David Jacques.

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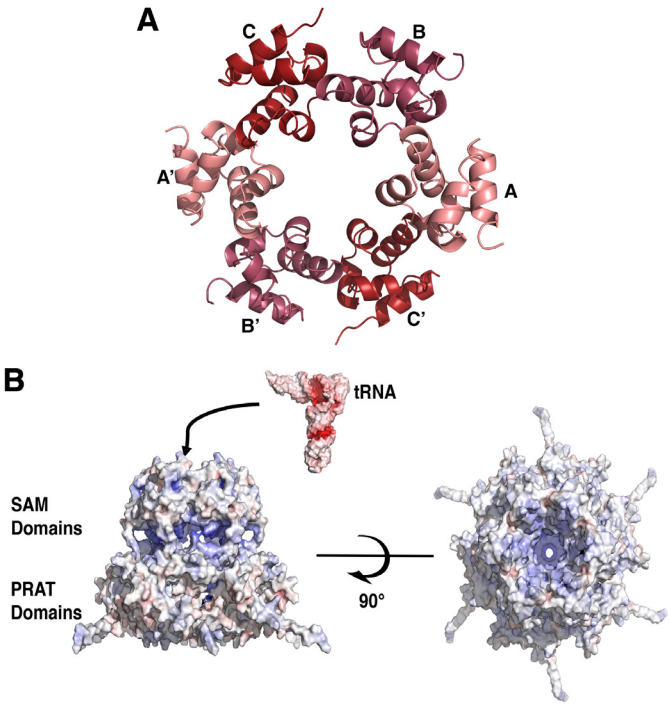
A Mitochondrial tRNA Importer

Olasz B[#], Smithers L[#], Evans GL, Anandan A, Murcha MW*, Vrielink A*. Structural studies of a mitochondrial tRNA import receptor. *J Biol Chem* 2024;300(5):107258.
[#]Contributed equally to this work
***Corresponding authors: alice.vrielink@uwa.edu.au, monika.murcha@uwa.edu.au**

Mitochondria are membrane-bound organelles in the eukaryotic cell that originated from an endosymbiotic event between an archaebacterium and a eubacterium. Most of the proteome required for mitochondrial function is nuclear encoded, translated in the cytoplasm and targeted to the organelle. Despite this, mitochondria retain a genome from their ancestral bacterial origin. This genome is actively transcribed and translated within the mitochondrial matrix, and is essential for mitochondrial function. Interestingly, the mitochondrial genome does not contain the full complement of tRNA with which to translate mRNA to protein, thus requiring specific nucleic acid importers. Tric1 and Tric2 (tRNA import component 1 and 2) had previously been identified by Murcha and colleagues (*Plant Physiol* 2016;172:2471–2490) as tRNA importers located in the outer mitochondrial membrane in *Arabidopsis thaliana*. Tric1/2 contain a N-terminal membrane-embedded PRAT (preprotein and amino acid transporters) domain, seen in many proteins involved in the transport of proteins and amino acids into mitochondria. Additionally, Tric1/2 contains a C-terminal SAM (sterile alpha motif) domain. SAM domains are small (65–70 amino acid) domains found in a diverse range of proteins, and are known to form oligomeric complexes through both homo- and hetero-SAM interactions, as well as protein–RNA complexes.

We determined the crystal structure of the SAM domain of Tric1 to better understand the features of the protein that facilitates tRNA binding and import. We observed a helical superstructure of six SAM domain monomers per helical turn in the crystal lattice (comprising two asymmetric units). Specific amino acids are involved in hydrogen bond and salt bridge contacts between the individual subunits. Using gel filtration chromatography, we observed a highly stable oligomeric species in solution, insensitive to heating at 95°C in Laemmli buffer. Mutagenesis and further structural studies tested the ability of the SAM domain to maintain an oligomeric form. Mutation of one of the salt-bridge forming residues (Asp235) to Ala did not affect the helical superstructure relative to the wildtype (WT) SAM domain. In contrast, mutation of Gly241 to Glu resulted in a different crystal packing arrangement and a lack of the helical superstructure. Gel filtration studies of the Asp235Ala mutant resulted in different sized oligomers, none of which were thermally stable as observed to the WT SAM domain, while the Gly241Glu mutant gave only monomeric protein. Thus, it was concluded that Asp235 and Glu241 are needed for oligomerisation and protein stability.



*(**A**) The superstructure formed by the WT Tric1 SAM domain corresponding to two asymmetric units in the crystal lattice shown from an axial view. The monomers are coloured in different shades of red. The monomers in one asymmetric unit are labelled as A, B and C and the corresponding monomers in the second asymmetric unit are labelled as A', B' and C'.*

*(**B**) Electrostatic surface representation of the AlphaFold2 predicted structure of full length Tric1 as a hexamer. The left panels show the side view of the hexamer and the right panels show the top view from the side containing the SAM domains. On the left panel, the electrostatic representation of a tRNA molecule has been included. Regions of positive potential are coloured in blue, and regions of negative potential are coloured in red.*

Studies of tRNA binding were also undertaken using electrophoretic mobility shift assays. While the WT SAM domain was able to bind tRNA, neither mutant nor double mutant (Asp235Ala:Gly241Glu) were able to show tRNA binding. To further understand the impact of these residues on protein function, complementation assays *in planta* were also carried out. *Arabidopsis tric1:tric2* knockout cell lines were complemented with WT Tric1 and the double mutant. The *tric1:tric2* knockout plants showed a developmentally delayed and chlorotic

phenotype, which could be restored by complementation with WT Tric1. In contrast, complementation of *tric1:tric2* knockout with the double mutant variant of Tric1 failed to restore defective growth characteristics. These results suggest that either Asp235, Glu241 or both residues are required for functional complementation *in planta* via tRNA binding, oligomerisation or both.

Finally, we used AlphaFold2 to further probe the oligomeric structure of full length Tric1. These *in silico* structure prediction studies showed that the full-length protein structure could be predicted with reasonably high confidence scores (pTM ~ 78). Predictions of different multimers of full length Tric1 were also undertaken and the highest confidence shown for a pentamer or a hexamer, both of which gave a cyclic, closed oligomeric species. The pentameric structure gave a central pore with a width of ~13 Å, at the position of the SAM domains while the hexameric structure resulted in a central pore has a width of ~20 Å. The electrostatic nature of the pore shows a highly positively charged surface throughout, which supports an expected pathway for a negatively charge tRNA molecule to pass through the oligomeric entity and cross the mitochondrial membrane. Intriguingly, a helical tRNA molecule is ~18 Å wide, of the appropriate dimensions to pass through a hexameric Tric1 pore. Based on these results, we propose that Tric1 forms a hexameric ring structure to facilitate the movement of tRNA across the mitochondrial membrane through a pore in the oligomeric assembly. Our current focus is to elucidate the structure of full-length Tric1 and better understand the mechanism of tRNA interactions and import.

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From left: Bence Olasz, Luke Smithers, Genevieve Evans, Anandhi Anandan, Monika Murcha and Alice Vrielink.

Unveiling the Mechanisms of Epigenetic Therapy in Breast Cancer: A 3D Genome Perspective

Achinger-Kawecka J#, Stirzaker C#, Portman N, Campbell E, Chia KM, Du Q, Laven-Law G, Nair SS, Yong A, Wilkinson A, Clifton S, Milioli HH, Alexandrou S, Caldon CE, Song J, Khoury A, Meyer B, Chen W, Pidsley R, Qu W, Gee JMW, Schmitt A, Wong ES, Hickey TE, Lim E, Clark SJ. The potential of epigenetic therapy to target the 3D epigenome in endocrine-resistant breast cancer. *Nat Struct Mol Biol* 2024;31(3):498–512.
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Epigenetic alterations play a pivotal role in cancer development and progression. Our recent studies have shed light on the intricate three-dimensional (3D) remodelling of the epigenome in breast cancer. Previously, we described that endocrine resistance in estrogen receptor-positive (ER+) breast cancer can be caused by epigenetic alterations at critical regulatory enhancer regions that prevent ER binding to the DNA (*Nat Commun* 2015;6:7758). More recently, we showed that development of endocrine resistance in breast cancer is also associated with disruption of the 3D genome structure, notably through long-range chromatin changes at ER-enhancer sites that become hypermethylated in resistant cells (*Nat Commun* 2020;11:320). In our new study, we delved into the potential of using epigenetic therapy, particularly focusing on the DNA demethylating agents decitabine (5-aza-2'-deoxycytidine), in combating endocrine-resistant ER+ breast cancer. Decitabine is approved by many international regulatory agencies, including the US FDA, European Commission and Australian TGA, for treating haematological cancers.

To delineate the mechanism of epigenetic therapy with decitabine, we assessed the molecular consequences of treatment on DNA methylation, 3D genome architecture and transcriptional programs in endocrine-resistant ER+ cancer cell lines and patient-derived xenograft (PDX) models. Our investigations unveiled a cascade

of events initiated by decitabine treatment, leading to profound changes in DNA methylation and 3D chromatin structure. By utilising PDX models, we demonstrated that decitabine induces DNA hypomethylation, resulting in the suppression of tumour growth and proliferation pathways.

We found that decitabine treatment resulted in DNA hypomethylation that was associated with 3D epigenome remodelling, highlighting the potential of epigenetic therapy in treatment of ER+ endocrine-resistant breast cancer. By integrating multiple layers of genomic data, including DNA methylation, transcriptome and chromatin binding profiles, we revealed a comprehensive picture of decitabine's impact on the 3D epigenome. Notably, decitabine-induced DNA hypomethylation leads to the activation of enhancers, gain in ER binding, rewiring of enhancer–promoter interactions, and subsequent activation of ER target genes involved in tumour suppression. By promoting enhancer activation and increasing enhancer connectivity, decitabine facilitates the formation of transcriptional hubs, ultimately restoring gene expression patterns disrupted in cancer.

Moreover, our research uncovered the direct role of DNA methylation in shaping the 3D genome organisation, emphasising its influence on chromatin structure and compartmentalisation. We found that decitabine treatment disrupted topologically associated domain organisation and A/B compartment structure, providing insights into how epigenetic therapies remodel the 3D landscape of the genome.

However, the study goes beyond conventional multiomics analyses by examining the genetic and epigenetic heterogeneity within tumours post-treatment. Surprisingly, we found that decitabine does not eliminate clonal diversity, indicating its ability to target a spectrum of tumour cells rather than a specific clone.

The study also explores the potential immunomodulatory effects of decitabine, highlighting its ability to upregulate immune pathways, which could contribute to its antitumour effects. Although the precise mechanisms are yet to be fully elucidated, the findings suggest a complex interplay between epigenetic reprogramming and the immune response in cancer treatment.

In summary, this research uncovers a novel molecular mechanism of epigenetic therapy in endocrine-resistant ER+ breast cancer, emphasising the importance of targeting the 3D epigenome architecture to overcome therapy resistance. Decitabine, through its ability to induce DNA hypomethylation and remodel 3D chromatin interactions, holds promise as a therapeutic strategy to reprogram gene deregulation and inhibit cancer growth.

Jo Achinger-Kawecka and Sue Clark
Garvan Institute of Medical Research

Epigenetic therapy (medicine in the bottle) has the potential to stop the outgrowth of endocrine resistant estrogen receptor positive (ER+) breast cancer cells by remodelling the 3D cancer epigenome to suppress the ER+ resistant cell growth (the noxious weed that can overtake and kill the rest of the plants in the garden).

From left: Top: Elyssa Campbell, Amanda Khoury and Qian Du. Middle: Joanna Achinger-Kawecka, Susan Clark and Clare Stirzaker. Bottom: Braydon Meyer, Ruth Pidsley and Jenny Song.

THOC2's Role in Neurodevelopmental Disorders: Insights from a Novel Mouse Model

Bhattacharjee R, Jolly LA, Corbett MA, Wee IC, Rao SR, Gardner AE, Ritchie T, van Hugte EJH, Ciptasari U, Piltz S, Noll JE, Nazri N, van Eyk CL, White M, Fornarino D, Poulton C, Baynam G, Collins-Praino LE, Snel MF, Nadif Kasri N, Hemsley KM, Thomas PQ, Kumar R#, Gecz J#*. Compromised transcription-mRNA export factor THOC2 causes R-loop accumulation, DNA damage and adverse neurodevelopment. *Nat Commun* 2024;15(1):1210.

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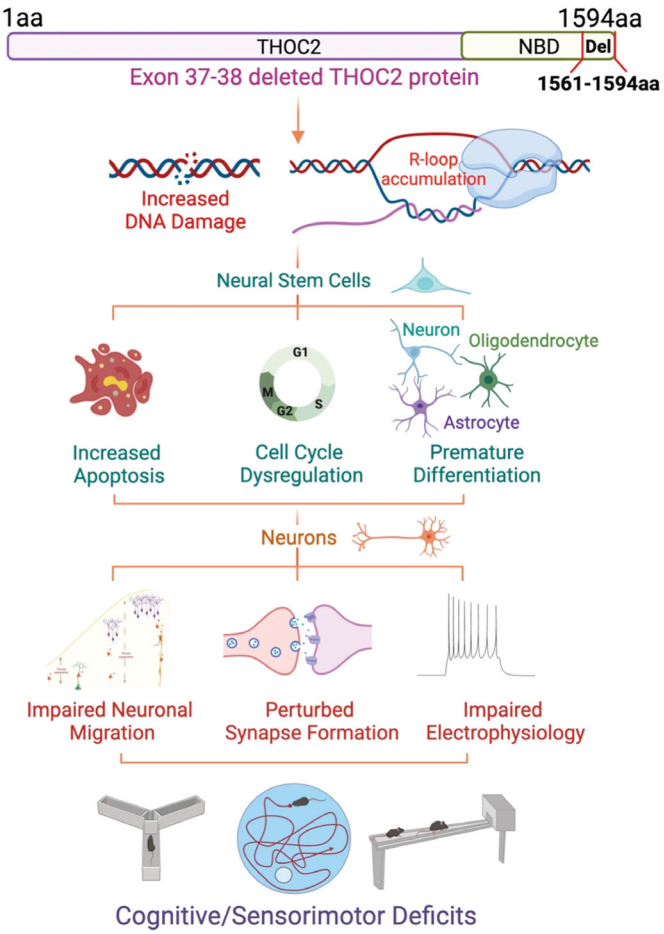
The human brain requires highly orchestrated gene expression to drive critical processes of its development and differentiation. As such, it is highly sensitive to even subtle changes in gene expression, often a consequence of genetic variation. This is exemplified by the knowledge of over 2,300 genes whose genetic variants lead to complex neurodevelopmental disorders (NDD). NDD gene variants impact numerous essential biological processes and their complete knockout can be embryonic lethal. One such example is variants in the X-chromosome gene *THOC2* that we were first to implicate in patients with clinically heterogeneous NDD presentations, now referred to as *THOC2* syndrome. *THOC2* encodes the largest subunit of the THO subcomplex and serves as a scaffold protein for the highly conserved TRanscription–EXport (TREX) complex. The multisubunit TREX, originally discovered as an mRNA export complex, has emerged as essential protein machinery for transcription, mRNA processing, preventing DNA damage and maintaining ESC self-renewal, pluripotency and differentiation during early embryogenesis. While many studies have provided insights into diverse roles of THOC2 protein, the findings were mostly from *in vitro* knockdown cells or knockout models involving lower organisms. The lack of a viable mammalian model, mainly due to *THOC2* gene essentiality, has been a major barrier to investigating the biological roles of THOC2 and more broadly the TREX complex, particularly in brain development.

We have collected over 60 partial loss-of-function *THOC2* NDD variants so far. While complete loss of *THOC2* can be lethal, we reasoned that hypomorphic (i.e., partial loss-of-function) variants from patients could offer a unique opportunity for generating an animal model for *in vivo* investigations. After unsuccessful attempts to generate mice with two different missense mutations, we successfully generated a preclinical *Thoc2* mouse model based on a hypomorphic *THOC2* patient variant that deletes the last two coding exons (i.e., exon 37 and 38) from the *THOC2* gene. We confirmed this by whole genome sequencing of the model animals. The embryos and adults of *Thoc2* exon 37–38 deletion male mice (called *Thoc2*$^{\Delta/Y}$) had significantly reduced weight (~15%) and smaller size compared to their *Thoc2*$^{+/Y}$ littermates, a phenotype like the exon 37–38 deleted patient. The P30 *Thoc2*$^{\Delta/Y}$ male mice showed a distinct shorter and flatter snout compared to the *Thoc2*$^{+/Y}$ mice. Extensive neurobehavioral testing showed that the *Thoc2*$^{\Delta/Y}$ male mice have learning, memory and sensorimotor deficits, recapitulating phenotypes observed in most of the *THOC2* syndrome patients. We found that the THOC2 protein is more abundant in embryonic stages and that a significant number of *Thoc2*$^{\Delta/Y}$ embryos die before



Schematic diagram showing the molecular, cellular and phenotypic consequences of Thoc2 *exon 37–38 deletion in the* Thoc2$^{\Delta/Y}$ *mice.*
Figure panel from Nat Commun *2024;15(1):1210 (CC-BY 4.0 license).*

blastocyst stage, establishing a critical role of THOC2/TREX in very early development.

The transcriptomic and proteomic data showed major dysregulation in pathways associated with transcription, splicing and higher order cognitive functions. The *Thoc2*$^{\Delta/Y}$ mice brains were smaller, particularly with a reduced ventricular zone associated with reduced neural stem cell (NSC) pool. Subsequently, we showed that *Thoc2*$^{\Delta/Y}$ NSCs undergo significantly higher apoptosis and have deregulation of the cell cycle, particularly at the G2/M phase. As the G2/M checkpoint is activated upon DNA damage, we found that *Thoc2*$^{\Delta/Y}$ mouse NSCs had higher amounts of damaged DNA. We found that this was due to significantly higher transcription associated triple stranded RNA:DNA:RNA hybrids (called R-loops) in *Thoc2*$^{\Delta/Y}$ NSCs. The *Thoc2*$^{\Delta/Y}$ neurons also showed increased DNA damage and impairments in neural structure and synapse formation leading to compromised electrophysiological properties. Similar DNA damage and R-loop accumulation was also evident in *THOC2* exon 37–38 deletion patient-derived dermal fibroblasts. Together, we have revealed a new mechanism of *THOC2* NDDs originating early in development and due to perturbed R-loop homeostasis in patient cells, and in stem cells and/or differentiated cells in *Thoc2*$^{\Delta/Y}$ mice. Our first mouse model for *THOC2/TREX* NDD patient variant provides excellent opportunities for understanding of the THOC2/TREX biology in stemness, development and differentiation as well as the clinical neuropathology of *THOC2* syndrome in the future.

Rudrarup Bhattacharjee,
Raman Kumar and Jozef Gecz
Adelaide Medical School & School of Biomedicine
University of Adelaide

From left: Back row: Lachlan Jolly, Nazzmer Nazri, Mark Corbett, Clare van Eyk and Alison Gardner. Front row: Jozef Gecz, Tarin Ritchie, Rudrarup Bhattacharjee and Raman Kumar.

Imputation of Plasma Lipid Species: Bringing New Life to Old Datasets

Dakic A, Wu J, Wang T, Huynh K, Mellett N, Duong T, Beyene HB, Magliano DJ, Shaw JE, Carrington MJ, Inouye M, Yang JY, Figtree GA, Curran JE, Blangero J, Simes J; LIPID Study Investigators; Giles G*, Meikle PJ*. Imputation of plasma lipid species to facilitate integration of lipidomic datasets. *Nat Commun* 2024;15(1):1540.
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The methodology of plasma lipidomic profiling has evolved over the last decade. The number, specificity, accuracy and precision of lipid measurements have increased due to improved chromatographic and mass spectrometric resolution of newer platforms. These improvements in lipidomic profiling have created new challenges to align lipidomic datasets created at different times or on different platforms. For instance, when designing lipidomic-based risk prediction models and validating them across different studies, analysts are faced with a difficult choice between building models with a reduced number of lipid species common to all datasets – thereby losing the rich detail of newer, better resolved measurements – or discarding older datasets altogether and accepting reduced validation potential.

In our recent work, we demonstrated a framework for harmonising such plasma lipidomic datasets with different coverage and levels of granularity in their lipid measurements. The principle behind our approach is a prediction (imputation) of unmeasured lipid species in older, less resolved datasets. This approach relies primarily on the stable correlation structure across plasma lipidomic profiles, found both within and between lipid classes (**Fig A**). This allows us to build accurate predictive models for individual lipid species, leveraging the high-resolution lipidomic profiles in a large reference dataset and use them to predict the

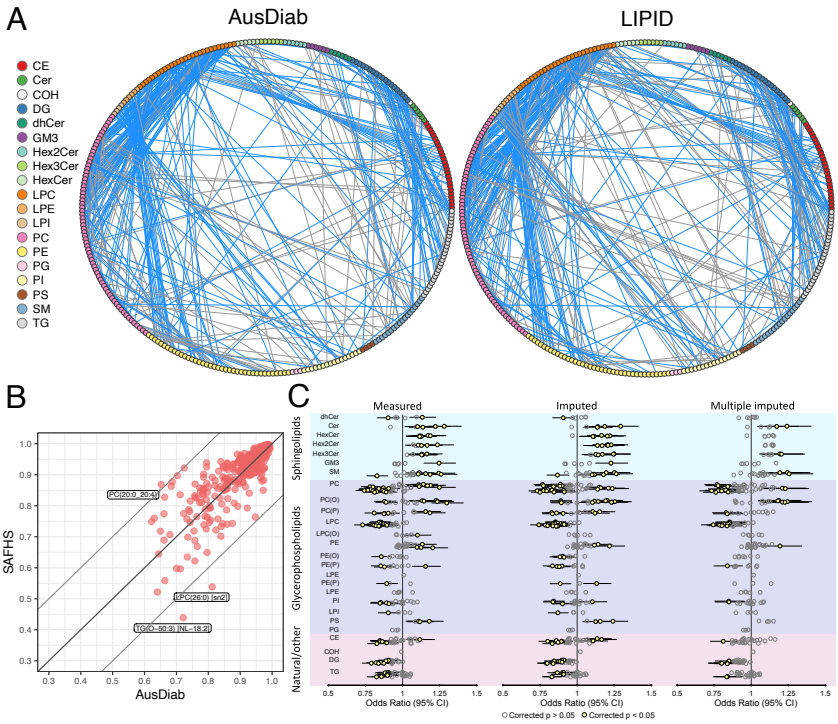
Publications with Impact

*(**A**) Partial correlation networks between lipid species in the AusDiab and LIPID studies, presented in a circle layout. Only lipids measured in both datasets were included in the analysis and the 1,000 strongest associations are shown for each dataset. 683 edges highlighted in blue appear in the top 1,000 edges in both correlation networks.*

*(**B**) Validation of lipid imputations in the SAFHS- predictive accuracy (r) in the AusDiab cohort was plotted against the SAFHS cohort (an ethnically distinct Mexican American cohort).*

*(**C**) Univariate association of measured and imputed lipid species with cardiovascular death.*

Figure panels from Nat Commun *2024;15(1):1540 (CC-BY 4.0 licence).*



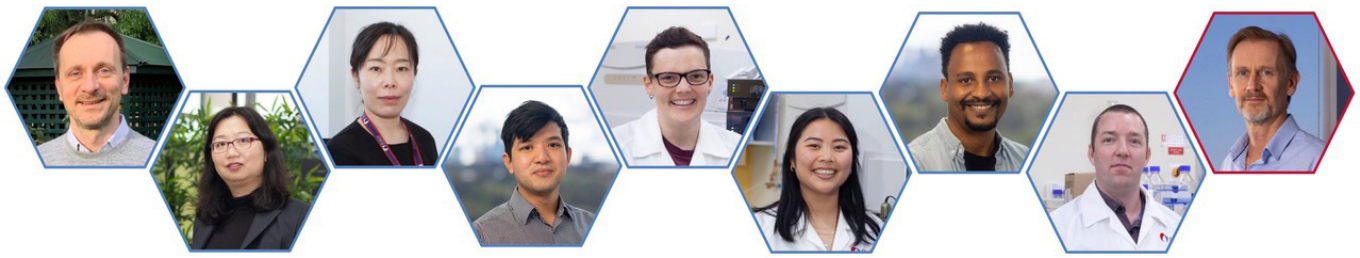
concentration of unmeasured lipid species in lower-resolution target datasets. Our method utilises elastic net prediction models and consists of several distinct steps: (1) construction of composite lipid measures in the reference dataset that map to the less resolved lipids in the target dataset, (2) identification and removal of discrepancies between aligned lipid species using the partial correlations, (3) generation of prediction models, (4) assessment of their transferability between the reference and target dataset, and (5) evaluation of their prediction accuracy.

To demonstrate our approach, we used a large reference dataset, the AusDiab cohort (n=10,339), profiled with a contemporary, comprehensive lipidomic platform (747 lipid species) to impute unmeasured lipid species in an older dataset, the LIPID study (n=5,991, two timepoints; 342 lipid species). We further validated lipid imputations in a second, ethnically distinct cohort, the San Antonio Family Heart Study (SAFHS; n=2,595). In addition to measures of predictive accuracy in the validation cohort (**Fig B**), we provided comparisons of the imputed and measured lipid species in terms of parameter estimation (**Fig C**) and predictive performance involving key clinical outcomes.

We have recently employed our imputation method to build and validate a lipidomic risk score (LRS) for cardiovascular disease (CVD). Our imputation method enabled a panel of lipids (n=142) missing in the Busselton Health Study (n=4,492) to be imputed, facilitating the validation process. We were able to demonstrate that the LRS significantly enhanced the stratification of intermediate-risk individuals, addressing a key challenge in CVD risk assessment. The LRS shows great potential clinical utility in selecting candidates for non-invasive imaging and other aspects of cardiovascular disease evaluation, prevention and management (Wu *et al., J Am Coll Cardiol* 2024, in press).

We believe that our new approach to harmonising plasma lipidomic datasets will facilitate data integration efforts creating new opportunities for meta-analyses and validation studies leading to wider utilisation of these valuable resources.

Aleksandar Dakic, Jingqin Wu, Tingting Wang, Kevin Huynh, Natalie Mellett, Thy Duong, Habtamu Beyene, Corey Giles and Peter Meikle
Baker Heart and Diabetes Institute



From left: Aleksandar Dakic, Jingqin Wu, Tingting Wang, Kevin Huynh, Natalie Mellett, Thy Duong, Habtamu Beyene, Corey Giles and Peter Meikle.

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Educator and Student Reflections on Supervising and Conducting Biochemistry Education-based Research

Jordan Witchard and James Tsatsaronis

Department of Biochemistry and Chemistry, La Trobe University

Universities across Australia and internationally increasingly employ academics in education-focussed (EF) positions that generally include a workload component for engaging in education-based research. However, distinct from the disciplinary research conducted by academics in teaching and research roles, research conducted by EF academics is less likely to be conducted as part of undergraduate Honours or graduate student research projects. The experiences of EF academics in supervising students, and the perspectives of students themselves, in conducting education research are also sparsely reported. As such, in this article we – an EF academic and undergraduate Science Honours student – describe our experiences of jointly conducting a biochemistry education research project. We frame these experiences as responses to three questions regarding our motivations in embarking on such a project, the challenges we have faced during the experience and advice we would give to others considering undertaking an education research project.

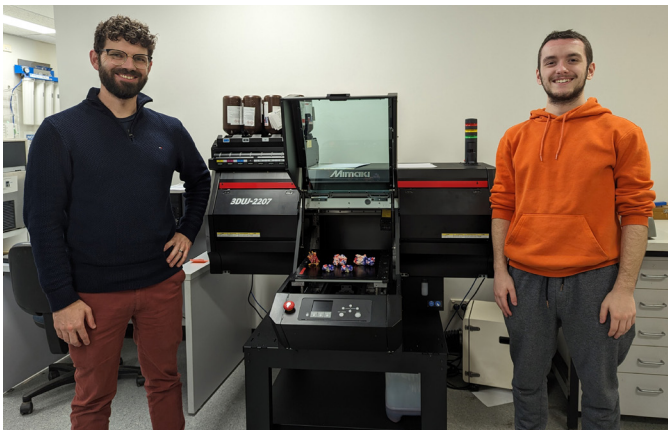

Fig. 1. *James (left) and Jordan stand next to a 3D printer used in the education-based research project.*

What motivated you to undertake/supervise an education project?

Jordan – After majoring in Biochemistry and Genetics, a project focused on education and theories behind teaching the concepts I had learned over my undergraduate studies seemed like a strange next step. As a high school student, I had poor grades and worse motivation. I then began studying biology where I encountered a teacher who was able to ignite a passion for biology, leading me to where I am today. I was further motivated by my continuing experience as a demonstrator for a First year biology class where I saw students 'get it', reinforcing to me why education is so important.

James – Being an EF academic and conducting education research provides a means to probe student learning in more than just a quantitative sense (i.e. impacting grades). Despite having a quantitative, molecular background, I've become more interested in how and why certain learning approaches work, or don't. Addressing these questions requires applying research approaches. Supervising a student researcher in this process means that I am not only accountable for this research for my own sake, but also for the sake of Jordan's project.

What challenges have you faced?

Jordan – I encountered a steep learning curve coming form an analytical background into a more qualitative data-oriented field. I felt deeply uncomfortable when reading science education focused literature as I found myself focusing on what I could immediately understand, i.e. effect and sample sizes rather than the informative qualitative data. Now, I'm beginning to adjust to these new challenges instead of needlessly clinging to what I had previously learned, I have turned my focus to learning skills that are more pertinent to education research.

James – Supervising an education Honours project has been a welcome challenge. From a logistical perspective, getting the project advertised, the ethics application and other paperwork ready in time is a constant juggle with other teaching responsibilities. However, another aspect which has been both a challenge and great source of joy, is actually defining a project and specific research question in the first place. It took much longer than I expected to dive into the literature to craft a meaningful research question and framework that we could use as a starting point.

What advice would you give to an EF academic or potential student considering an education project?

Jordan – Some general advice I would give to students transitioning from molecular science to science education would be to first get experience in teaching (in any capacity) so that you can learn and develop the skills

relevant to an education project. Second, I encourage reading outside of your own field more often and getting used to different techniques and philosophies between fields. Finally, develop a good relationship with your supervisor – I would not have adjusted as well to this new field without the mentorship of my supervisor, James.

James – Following on from my earlier point on defining a research question, I'd advise EF academics and potential students to start early when trying to decide what your project will address. As Jordan said, read as widely and as deeply as you can from the literature, and find academics from disciplines outside your own who can provide input. On that point, don't hesitate to collaborate with others or to invite colleagues to be a 'critical friend' for your project. Finally, be realistic in terms of what can be achieved in the scope of a student project but keep an open mind to what potential future projects could extend from it.

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Premeditated Blunders to Trigger Cognitive Learning in Biochemistry: Perceptions of Undergraduate and Postgraduate Students Pursuing Medical Sciences

Sheethal Mohan[1], Chandrika Nayak[2] and Ullas Kamath[2]
[1]Department of Anatomy and Physiology, University of Melbourne
[2]Department of Basic Medical Sciences,
Manipal Academy of Higher Education, Manipal, India

Innovative teaching strategies in lectures that promote student active learning are of utmost importance. An effective strategy to enhance student engagement is to introduce cognitive conflict. Cognitive conflict is defined as a teaching strategy where students are presented with information that is contradictory to their understanding (1). Cognitive conflict can be introduced to students through 'blunder lectures' (BL), where the lecturer purposefully delivers incorrect information to students (2). BL have previously been introduced to first year undergraduate (UG) students studying medicine in tutorials in the field of physiology (1) and anatomy (2), and in small-group tutorials (3).

In biochemistry, BL have been successfully implemented to students by Dean and Professor of Biochemistry, Dr Ullas Kamath (Melaka Manipal Medical College), across all his lectures for the past three decades. Examples include usage of statements such as "glucagon is a storage polysaccharide," "insulin is a steroid hormone," "pyruvate in aerobic conditions is converted to lactose" and "lipoprotein that delivers cholesterol to extrahepatic tissues is LDH." Another example of a 'blunder' stated in a lecture is provided in **Fig. 1**. The 'blunders' were made on fundamental concepts and were later clarified at the end of lecture as a method to reinforce concepts.

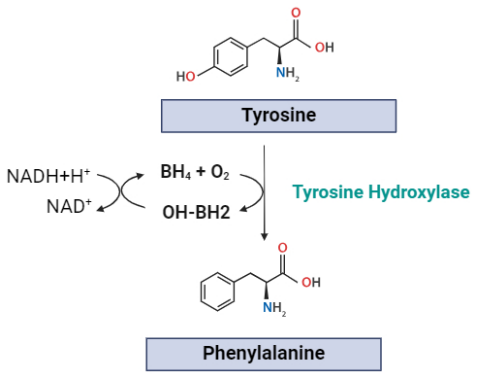

Fig. 1. *Synthesis of phenylalanine from tyrosine in humans. Created in BioRender.*

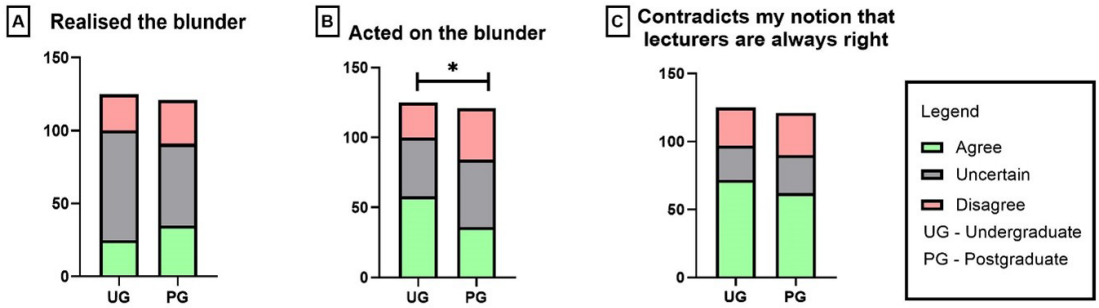

Fig. 2. Domain 1: Student perceptions of BL as a learning experience.
Questionnaire data in Domain 1 was analysed using chi-square test. UG n=125, PG n=123.
(A) Realised the blunder, *with uncertainty in UG (60.0%) being higher than PG (46.3%).*
(B) Acted on the blunder *where overall there was agreement on acting on the blunder, but with UG students being more proactive (46.4%) than PG students (29.7%), (p<0.05).*
(C) Contradicts my notion that lecturers are always right *with overall agreement among UG (57.6%) and PG (51.2%).*

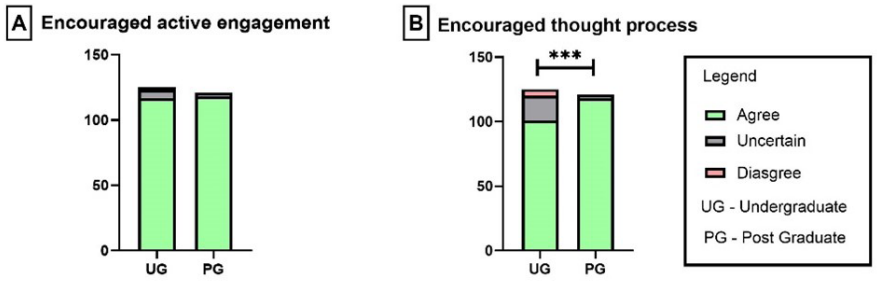

Fig. 3. Domain 2: Perceptions of BL on learning during lecture.
Questionnaire data in Domain 2 was analysed using chi-square test. UG n=125, PG n=123.
(A) Encouraged active engagement *with greatest overall agreement in both UG (93%) and PG (97.5%)*
(B) Encouraged thought process *where UG agreed (80%) while PG were in greater agreement (97.5%), (p<0.001).*

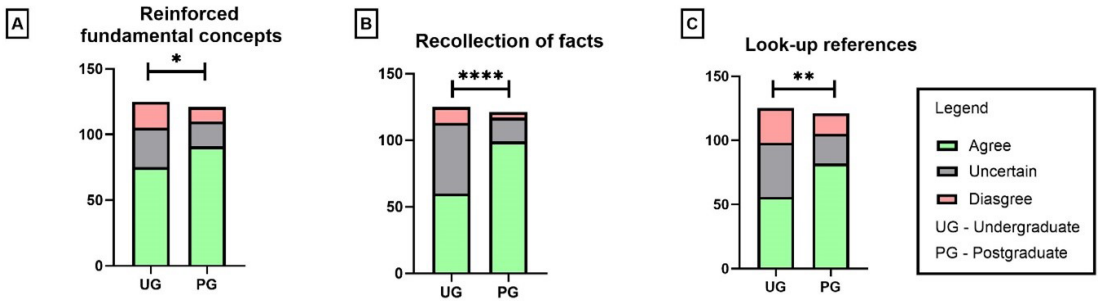

Fig. 4. Domain 3: Perceptions of BL on learning post-lecture.
Questionnaire data in Domain 3 was analysed using chi-square test. UG n=125, PG n=123.
(A) *Reinforced fundamental concepts with overall majority agreement among UG (60.0%) and PG (75.2%), (p<0.05).*
(B) *Recollection of facts clearly establishes a difference in opinions with UG agreement (48.0%) while PG are in greater agreement (81.8%) (p<0.0001).*
(C) *Look-up references with UG in lesser agreement (44.8%) than PG (67.77%) (p<0.001).*

In our current study, BL were delivered in various topics of medical biochemistry to first-year UG medical students from Melaka Manipal Medical College, Manipal, India, and first-year postgraduate (PG) students of Master of Medical Sciences from Kasturba Medical College, Manipal University, India. Both cohorts received at least ten hours of BL. Answers to a questionnaire were obtained from participants at the end of their first-year studies, with ethics obtained from the institutional Ethics Committee. The questionnaire was divided into three domains as described below with the results provided in **Fig. 2, 3 and 4**.

The overall acceptance of this teaching strategy has been heartening. The uncertainty in realising the blunder for UG students seems to be higher and maybe attributed to their lack of fundamental knowledge in the field compared to PG students. It is interesting to note that, although UG students were mostly uncertain about being able to identify the blunder, they were more proactive in acting upon the blunder by questioning the lecturer. PG students were less trusting of the lecturer's knowledge, which could be attributed to more self-directed study requirements as a PG or familiarity with the Professor's teaching strategy.

This current teaching strategy, as perceived by both UG and PG students, is an encouraging active engagement strategy and a thought process promoting session. Post-lecture, both UG and PG students agreed that BL helped reinforce their fundamental biochemistry knowledge, their recollection of facts and encouraged them to look at more reliable sources of information; though PG students seemed to benefit more post-lecture from BL as indicated in domain 3.

Of note, two of the co-authors of this article were PG students of this Professor and have been inspired to inculcate this approach to teaching effectively in their own teaching practice.

The concept of BL has the potential to be used in formative assessments to enhance metacognitive skills in students. Furthermore, the role of BL may be introduced in lectures to enhance student engagement in an age where recorded lectures are gaining popularity.

Were you able to spot the blunder in Figure 1?

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Issue	ASBMB Content	Copy Deadline	Issue Date
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August 2024 55(2)	Nominations for medals, awards and fellowships Notice of AGM/proposed constitutional changes	Monday 3 June	Monday 29 July
December 2024 55(3)	Annual reports ASBMB meeting report	Monday 7 October	Monday 2 December

Fixing the Kinks in the COIL of Work Integrated Learning

Jessica Borger[1,2,3], Megan Taylor[1,2] and Kyoko Hombo[4]

[1]Walter and Eliza Hall Institute of Medical Research

[2]Department of Medical Biology, University of Melbourne

[3]Central Clinical School, Monash University

[4]Osaka University, Osaka, Japan

Ensuring real-world relevance in the curriculum not only equips students with practical skills, it also nurtures global citizenship among graduates, enabling them to thrive beyond the classroom. Job readiness often relies on pedagogical approaches like problem-based learning and authentic assessment to integrate real-world scenarios into learning to foster critical thinking, problem-solving, and intercultural competencies (ICC) (1,2,3,4). Open pedagogy (including work integrated learning (WIL)) involves authentic student engagement, which amplifies this real-world teaching (5). WIL provides the means to 'do in context', rather than developing practical skills isolated from the situations in which the student will be expected to use them, yet many WIL programs overlook global teamwork.

The COVID-19 pandemic accelerated the use of digital technologies in education, expanding curriculum possibilities to include global perspectives. Consequently, employers now seek graduates proficient in their fields and capable of thriving in cross-cultural environments, valuing intercultural communication and virtual teamwork skills. Collaborative Online International Learning (COIL) programs offer opportunities for active academic and professional skills development across borders, fostering intercultural competencies.

Our joint Translational Medicine and Biomedical Entrepreneurship (TMedBiomE)-COIL PhD program between Monash University and Osaka University demonstrates how the development of international knowledge, pedagogical knowledge and the linkage between the two is key for successful WIL and internationalisation of the curriculum.

The TMedBiomE-COIL program facilitated comparative learning between Translational Research PhD students at Monash University and students in Osaka University's Biomedical Entrepreneurship and Innovation program (**Fig. 1**), with the aim to foster global scientific exchange through synchronous and asynchronous online group

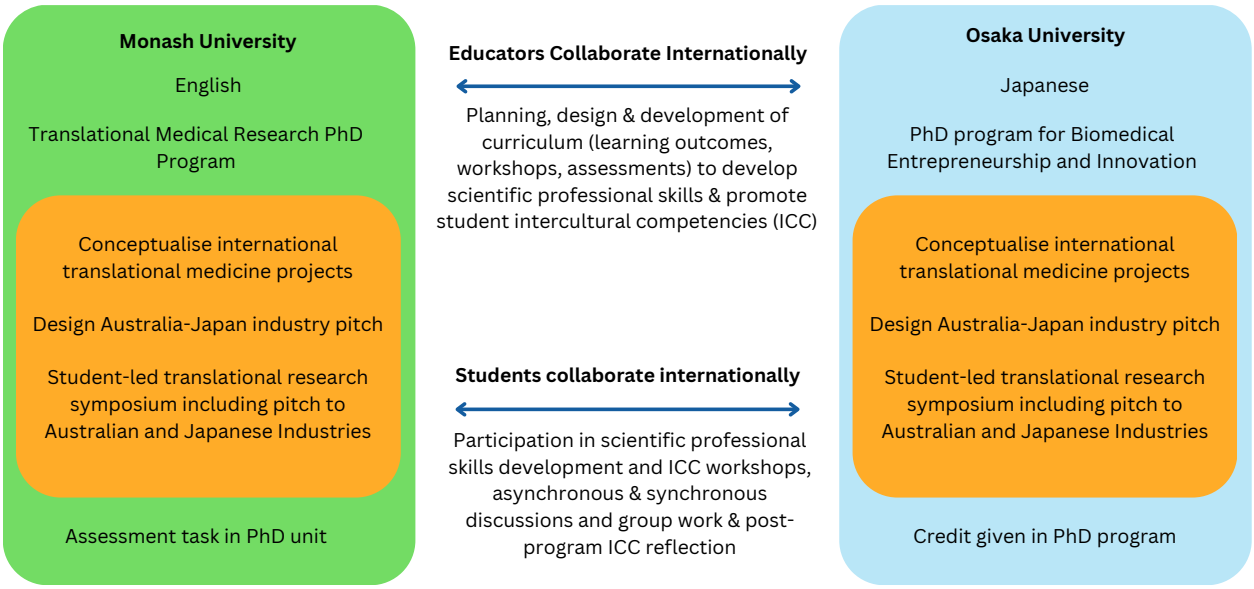

Fig. 1. TMedBiomE-COIL pilot program between Monash University and Osaka University. *A shared syllabus was developed within the COIL program of the Translational Medical Research PhD program at Monash University and the PhD program for Biomedical Entrepreneurship and Innovation at Osaka University (TMedBiomE-COIL) to support both educators and students in international collaboration, development of skills and enhancement of intercultural competencies.*

work. COIL was embedded as a course requirement for Monash students, with corresponding credit awarded to Osaka students. A shared syllabus was developed with COIL workshops including a Monash-run session focusing on poster design and presentation, and an Osaka-run session on pitching scientific concepts to industry. Small groups conceptualised translational medicine projects, pitching them to pharmaceutical industries in Australia and Japan. Students compared healthcare needs and pharmaceutical industries between Australia and Japan, presenting their projects in a student-led symposium focusing on research enterprise and market considerations. The program aligned with WIL outcomes, ensuring graduate students actively contributed to global medical practice and professional development, which is also reflective of internationalisation of the curriculum.

In addition to developing scientific research skills, the development of ICC was critical, an aspect often overlooked in conventional WIL initiatives. ICC encompasses one's "ability to interact effectively and appropriately in cross-cultural situations based on his or her intercultural attitudes, knowledge, comprehension, and skills" (6), an essential attribute in a COIL classroom for both students and academics. Recognising its significance, we integrated three ICC activities before students engaged in scientific WIL.

First, a 'Where were you?' icebreaker activity fostered discussion around meaningful years in our lives, revealing diverse perspectives shaped by cultural, geographical and religious backgrounds. The DISC® leadership test and intercultural conflict style inventory prompted students to reflect on their leadership and conflict resolution styles, as well as consider those of all members of the group, through a cultural lens.

The purpose of the embedded activities was to build leadership skills with an intercultural focus, mirroring real-world global research teams. Post-survey data indicated that students had enhanced confidence in ICC groupwork (**Fig. 2a**) resulting from synchronous and asynchronous online international groupwork, as well as leadership training and intercultural competency workshops. Furthermore, students reported improved awareness of ICC differences and barriers (**Fig. 2b**), and improved communication adaptability to accommodate cultural differences (**Fig. 2c**). These results, and other unpublished data, suggest that COIL programs are valuable additions to the curriculum, to provide students with the training and tools required to work inclusively and equitably in intercultural settings.

The TMedBiomE-COIL program enhanced students' scientific expertise and cultivated essential interpersonal skills required to thrive in diverse, cross-cultural environments within the global community. By introducing an international virtual dimension to partnered translational biomedical PhD programs through a shared syllabus, the TMedBiomE-COIL program fostered academic learning experiences that

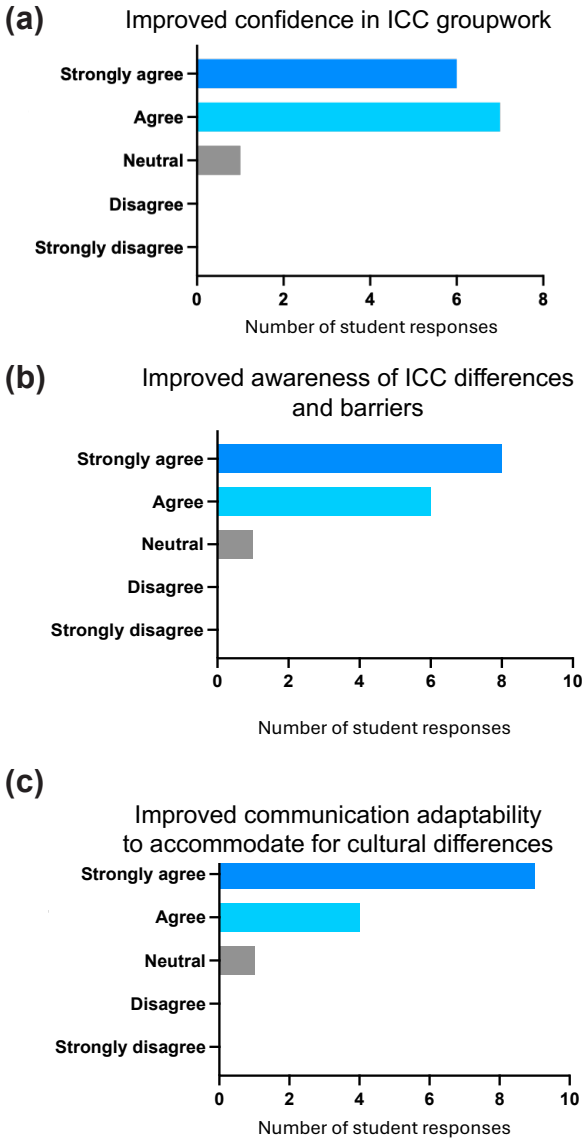

Fig. 2. COIL workshops to teach ICC improved students' abilities to participate in group work within virtual global classrooms.
*Post-survey data from Monash and Osaka University demonstrated that following participation in the COIL program students had (**a**) improved confidence in approaching ICC groupwork, (**b**) improved student awareness of and ability to identify differences and barriers in intercultural group work and (**c**) improved communication adaptability to accommodate cultural differences.*

developed intercultural competence. To effectively prepare science postgraduates for today's global healthcare landscape, WIL strategies must raise awareness of cultural differences in communication, leadership and conflict resolution. This requires internationalising the curriculum through student mobility programs, international partnerships and embedding intercultural competency development (7,8,9). Merely diversifying student cohorts is insufficient, instead it is imperative to develop engagement strategies that

foster intercultural competencies (7,10,11,12,13) whilst providing real-world academic learning situations. COIL programs, such as those described, are essential for advancing WIL and work-ready, inclusive and equitable global citizens.

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SDS Page: Short Discussions for Students Page

Best Practice for Writing Travel Grant Applications

Pirooz Zareie

Doherty Institute

In my opinion, one of the best things about a career in academia is the travel opportunities. Great science rarely happens in isolation, and certainly not within borders! Travelling nationally or internationally to attend a conference or to visit a lab can be a very rewarding and fun experience, plus it is great for your academic profile and career.

International conferences will often invite established and emerging global leaders to give plenary talks, which is a great opportunity to hear from them and keep up with the latest research in your field. If you are looking to join a new lab, conferences are a great way to discover potential lab groups and areas of research in which you might want to work in the future.

Here, I reflect on some past experiences and share some tips on how to write a travel grant application.

Finding travel grants

There are multiple avenues and agencies through which you can apply for travel grants. Your first point of call is probably the conference you are interested in attending. Many conferences will offer travel awards to attend the conference – this is usually based on the quality of the abstract you have submitted, so take some time to write one that will get the reviewers excited!

After this, the next option is through your university or research institution, most of which will offer travel awards to PhD students or ECRs to present their research. Within your institute, funding can even come from multiple levels, such as through faculty or departmental schemes and it is important you look for as many of these as possible to increase your chances of success.

Other great sources of travel grants are through memberships of scientific societies such as the ASBMB. If you are a member of multiple societies, then you will have even more access to travel grant opportunities. In my experience, these have been the best sources for travel awards!

Preparing your application

Eligibility and Guidelines

Start preparing early! Begin by thoroughly understanding the eligibility requirements and guidelines provided by the funder. This foundational step is crucial. Ensure you meet all criteria and follow any specific instructions. Many of these travel grants may require a letter of support from your supervisor and they will probably not appreciate a last-minute request for this!

Pro tip: Draft the support letter yourself. Don't worry, this is not cheating! Your supervisor doesn't know your CV back to front, so it's very helpful for them if you can highlight the key points that might benefit your application.

Target Audience and Purpose

When writing your application, it is important to consider the purpose of the grant and who is likely to review your application:

Promoting collaborations

If the grant aims to foster collaborations, highlight how attending the event will facilitate networking and knowledge exchange. If you are planning to meet with any international speakers at the conference, then highlight those people/meetings in your application! This would be very impressive.

Learning new techniques

If the grant supports skill development, emphasise how the event will enhance your expertise. This is particularly important if you plan to visit a lab.

Oral presentation

If the grant is for disseminating your research and promoting your profile, explain how your participation will contribute to the conference or meeting. Highlight how your abstract and research topic is aligned with the conference focus. If it is a specialised meeting, highlight to your reviewers why this meeting will be the most beneficial to your career.

Value for money

Many travel grants are intended for promoting a student's or ECR's career, research profile and/or dissemination of research. Because of this, I would think about any potential labs/institutes that you are interested in visiting, within reasonable travel from the conference. Reach out to them and ask about any opportunities to give a seminar. Just don't leave it to the last minute to ensure you can be added to their seminar programs.

I would highly encourage doing this! Some of the best and most productive talks and networking I have experienced were always in smaller settings, e.g. during a lab visit or seminar. The benefits of doing this are twofold. You will have a hand-picked platform to present your research internationally, which is great for your

SDS Page: Short Discussions for Students Page

profile, and you will also get to visit and meet the lab that you may be interested in joining. This is great value for money and is likely to be viewed positively by the travel grant funder.

Craft a Compelling Narrative

Within the application guidelines, create a persuasive narrative. Clearly articulate why attending this conference is essential for your professional growth and address how it aligns with both your goals and research interests and the purpose of the grant.

Career benefits

Describe how the grant will benefit your career. Will it expand your network, enhance your skills or open new opportunities? Be specific and highlight the long-term impact.

Research impact

Discuss how attending the event will impact your research. Will it lead to collaborations, data collection or exposure to cutting-edge developments? Show the direct link between the grant and your research goals.

Supporting documents

Don't overlook supporting documents. Again, start early!

a. **Scientific abstract:** You might need to submit a scientific abstract with your travel grant application, particularly if you are applying for a grant to attend a conference. Prepare this early and, if possible, get some feedback from your supervisor(s).
b. **Letter of support:** If required, secure a letter of support well in advance. Supervisors can be very busy. Don't leave this crucial step to the last minute.
c. **Scientific CV:** Keep your CV concise and relevant. Highlight relevant research, publications and any previous grants or awards. Aim for a balance between your most impressive and most recent achievements.

Remember, travel grants are usually highly competitive. Don't be down on yourself if your application is unsuccessful. Like most people, I have had many more unsuccessful applications than successful ones! Make the most of what you have done:

- Organise and store your written applications in a folder. This will form the bones for your next applications and save you a lot of time.
- Keep a live CV and update it as often as possible. This will also save you time.

Finally, good luck!

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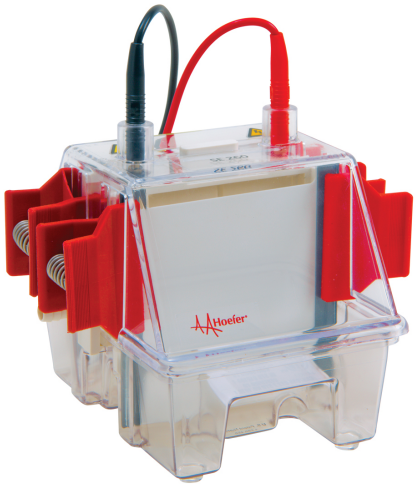

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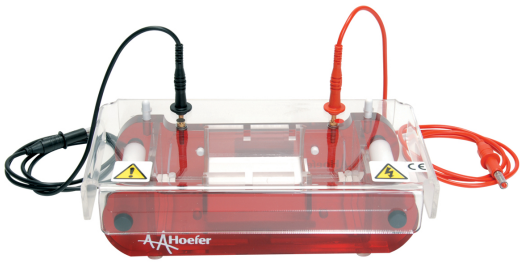

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Off the Beaten Track

Written by former researchers who have now established careers outside of research, Off the Beaten Track is intended to give the readers insights into the range of alternative careers available to them. Authors describe the paths they have taken to arrive at their present career and provide a detailed description of exactly what the job entails on a day-to-day basis.

Engaging Minds: A Neuroscientist's Path to Educational Excellence and Engagement

Keely Bumsted O'Brien, Project Manager, Education and Engagement, Olivia Newton-John Cancer Research Institute

"I love science and research. I love talking about it, doing it and teaching it. Nowadays, my engagement in science and research remains, it's just outside the lab."

Keely Bumsted O'Brien.

My career in science began at the end of my first undergraduate year at Simmons University in Boston, Massachusetts, USA, when I decided that an English and Education double major was not for me. I had been bitten by the science bug leading me to transfer to Biology. Graduating with a Bachelor's in Biology with distinction in 1991 opened the door to a PhD at the University of Washington in Seattle. My thesis research investigated the development of the morphologically and functionally specialised macular region in the retina associated with high visual acuity at the centre of gaze. Post PhD, between 1996–2010, I stayed focussed on vision research and travelled the world, undertaking postdocs at Yale University and Max Plank Institute, lectureships at University of Auckland, and an ARC Centre of Excellence Senior Research Fellow position at the the Australian National University (ANU). My career shifted in 2010 when I had an epiphany that I enjoyed teaching science, talking about science and asking research questions about how to train scientists more than working at the bench. I couldn't shake the feeling that my skills were more impactful outside of the lab. The perfect opportunity for a change arose when for family reasons, I left ANU and moved to Melbourne.

After investigating the job market and looking for opportunities that would allow me to develop my science education skills, I accepted an academic teaching focused position at the Walter and Eliza Hall Institute (WEHI). As Head of the Scientific Education Office (2010–2022), I developed my skills and networks to support Honours teaching through the Department of Medical Biology, University of Melbourne along with researcher development. The Honours coursework underwent a slow evolution during my time with major changes approved by the University of Melbourne Academic Board. In 2013, I conceived, designed, pioneered and led a coherent graduate researcher Development Program at WEHI. In 2016, I was awarded a Senior Fellowship in the Higher Education Academy in recognition of my teaching innovations, ongoing impact and influence.

In 2023, I joined the Olivia Newton-John Cancer Research Institute (ONJCRI) as Project Manager, Education and Engagement. At ONJCRI, I have used a consultative evidence-based approach to design and develop a bespoke Learning and Development Framework and Program. Used in conjunction with a redesigned Progress Review and Career planning tool that I developed in late-2023, the competencies outlined for each capability provide a scaffold for learning opportunities allowing researchers to consider and chart their development needs. In addition, I have designed a bespoke formal consumer (individuals with lived experience with a disease) program to enhance researcher and consumer engagement. Finally, I am using my skills to enhance and promote the student experience at ONJCRI.

I never get bored in my current role. There is always something to learn, new people to meet and creative projects to plan. Day-to-day, I could be doing

Off the Beaten Track

anything from meeting with stakeholders (consumers, researchers, students, research support staff, etc) to discuss their needs related to the various projects I'm managing, to preparing presentations or developing evidence-based programs. I get to read the literature, engage in critical thinking, prepare funding applications and design workshops/learning programs. My areas of interest intersect with lab-based programs, which allows me to keep a finger on the pulse of scientific research, especially as it relates to staff, students and consumers.

Because I'm still asking questions, doing thought experiments and a bit of research, the skills that I learned during my lab-based training have been highly transferrable. The organisational and project management skills that were so essential to successfully executing a scientific program, doing experiments and running a lab, now allow me to be a highly productive person who multitasks with ease. My current work requires high-level written and verbal communication skills that were born in grant writing and scientific presentations, and further honed by my subsequent roles.

I love what I do; it fulfills my curiosity, my desire to teach and develop a body of work. The challenges that come with my role involve scope creep (the project grows beyond its original goals), poorly defined requirements (everyone has to clearly be on the same page), schedule restraints (you want me to do what by tomorrow?) and budget with workforce needs (you need the money and the people to do the work). Project management and stepping outside of the traditional academic setting does have a degree of uncertainty, but the rewards of being fulfilled by a role outweigh this challenge.

Whenever I am asked to give career advice, I automatically say, "Do what you love." Sounds impressive, but is not always helpful, so here is some more concrete advice:

1. You are not a failure if you leave the lab. So much of science requires translation, commercialisation and education, to name three of many, many areas, that your contribution even if it's not in the lab will be sought after and valued.
2. Be curious, be brave and be informed. Explore your options, have informational interviews and make informed choices.
3. Stop calling careers outside of the lab, alternative careers. Just call them all careers. Many careers use the skills and knowledge developed during PhD training.
4. Make your own opportunities. "Opportunities don't happen, you create them" – Chris Grosser.
5. Mentorship is invaluable, regardless of whether you are the mentor or the mentee. If you don't have a mentor, go get one!
6. It's OK to change direction. We all grow and evolve as people. Forge a career doing what you enjoy. Do what you love.

Keely.BumstedO'Brien@onjcri.org.au

Perth Protein Group: an ASBMB Special Interest Group

The Perth Protein Group (PPG) is now in its fifth year. In 2023, the Executive Committee for the PPG was Mark Agostino (Chairperson), Joel Haywood (Treasurer), Tahlia Bastholm (Secretary) and Josh Mylne (Webmaster). There were also four Events Officers, Aleshanee Paxman, Andrew Marshall, Brady Johnston and Farley Kwok van der Giezen. We held our 2023 AGM at the University of Western Australia Albany campus. Albany is a port city about 400 km south of Perth with a population of approximately 35,000. A popular stop off on the way was the Williams Woolshed providing a welcome respite from the long journey south and a crucial EV charging point. We stuck to the format of our first AGM, similar to the long-running and successful SPG/QPG East Coast Protein Meeting. Most delegates arrived on the Friday afternoon 3 November, and we opened proceedings with

Perth Protein Group: an ASBMB Special Interest Group

Delegates at the 2023 Perth Protein Group AGM at the University of Western Australia campus in Albany.

a keynote session by Dr Gavin Knott, titled Harnessing Microbial Dark Matter for Biotechnology. This was followed by a session of four more talks, before drinks and then dinner. Saturday included seven talks, starting with Professor Phoebe Rice from the University of Chicago and an industry session held by our sponsor, Cytiva. The program included sessions entitled Biological Chemistry, Biochemistry and Chemical Biology. The day ended with a poster session and the conference social at Due South in town. On the Sunday, we had one last session that showcased four early- and mid-career research talks. The day was closed out by awarding some prizes. There were two winners, each taking home a $200 prize: Anna Faber (Best Student Talk) and Brady Johnston (Best EMCR Talk), both sponsored by Cytvia.

Registration remained at the very low rate of $60 for the early birds. We plan to continue using university campuses that are ideal for small conferences, provide a getaway and are usually very affordable. The venue for PPG 2024 is yet to be decided but will likely be at a Perth campus, with remote campus retreats occuring biannually.

Our most recent event was a special presentation by Professor Pavel Pevzner from UCSD, USA, titled Computational Natural Products Discovery: From Peptidogenomics to Genome Mining to Spectral Networks, held at the University of Western Australia on 24 March 2023. More recently, we have begun a monthly newsletter dedicated to showcasing the outstanding research publications of EMCRs and group leaders within our community. The primary goal of this newsletter is to cultivate collaborative efforts among our members and establish connections before our annual general meeting. Our database contains 170 current members. To be added to our database and kept up to date on PPG activities, email us at the address below.

Joel Haywood, Curtin University
Chairperson, Perth Protein Group
Email perthproteins@gmail.com
Website https://www.perthproteins.org

PPG members showcased since the PPG newsletter began in January 2024.
Top (from left): Amr Arishi (Chemical Science), *Lois Balmer* (PNAS Nexus *and* BMC Public Health), *Brendan Chapman (Forensic Science International), Catherine Colas des Francs-Small* (Plant Physiology), *Melissa Eccles* (FASEB) *and Anna Faber* (FEBS Journal).
Bottom (from left): Adam King (Journal of Chromatography A), *Kim Melville and Muhammed Kamran* (Current Biology), *Georg Fritz* (BioDesign Research), *Sneha-Priya Pappula-Reddy* (Environmental and Experimental Botany) *and Chunbin Zhou* (Non-coding RNA Research).

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NOMINATIONS FOR MEDALS AND AWARDS

*The **Lemberg Medal** is awarded to a distinguished ASBMB member who will present the Lemberg Lecture at the ASBMB annual scientific meeting. The Medal is presented in memory of Emeritus Professor M.R. Lemberg who was the Society's first President and Honorary Member. The award will be made to an individual who has demonstrated excellence in biochemistry and molecular biology and who has made significant contributions to the scientific community. An honorarium is provided by ASBMB.*

*The **Shimadzu Research Medal** is awarded to an outstanding ASBMB member with no more than 15 years since the award of the PhD degree (or equivalent taking any career disruption into account) at the nominated deadline. The successful candidate will present the Shimadzu Medal Lecture at the ASBMB annual scientific meeting. An honorarium is provided through the courtesy of Shimadzu.*

ASBMB Awards 2025

APPLICATIONS FOR TRAVEL AWARDS AND FELLOWSHIPS

*The **Eppendorf Edman ECR Award** is awarded to an ASBMB member with no more than 7 years postdoctoral experience (or equivalent taking any career disruption into account), in recognition of their outstanding research work. The Award provides funds to assist the recipient to attend an overseas conference in a field associated with biochemistry or molecular biology or to visit briefly a research laboratory in Australia or elsewhere to access specialised equipment or to learn new research techniques. The recipient will give a talk at the ASBMB annual scientific meeting. The contribution to travel expenses is provided through the courtesy of Eppendorf South Pacific.*

*The **SDR Scientific Education Award** rewards outstanding achievement in education in biochemistry or molecular biology, especially innovation and creativity in education, with a view to fostering leadership in this important area of the Society's objectives. The Award will enable the recipient to participate in an international conference with a significant focus on education, or to spend a period of time at another institution for the purposes of undertaking developments in education in biochemistry and molecular biology. The recipient will present a lecture within the Education Symposium at the ASBMB annual scientific meeting. The contribution to travel expenses is provided through the courtesy of SDR Scientific.*

*The **Boomerang Award** is awarded to an outstanding expatriate Australian biochemist or molecular biologist to allow them to return to Australia to present their work in a symposium the ASBMB annual scientific meeting and to give seminars at universities or research institutes. This will provide the awardee with exposure in Australia and will facilitate interactions with local researchers. The Award makes a significant contribution to the cost of a return airfare and accommodation for the ASBMB annual scientific meeting, and towards domestic travel expenses to visit at least one other Australian city. Applicants must have been awarded their PhD not more than 10 years prior to the closing date (or equivalent taking any career disruption into account). The contribution to travel expenses is provided by ASBMB.*

*The Awards Committee will also award several **ASBMB Fellowships** to postgraduate students who are no more than 2 years prior to the completion of their PhD degree or recently graduated postdoctoral researchers no more than 2 years subsequent to the award of their PhD degree. The contribution to travel expenses is provided by ASBMB. The most outstanding ASBMB Fellowship applicant may receive the **Fred Collins Award**. These travel grants are awarded to early career researchers, normally resident in Australia, in recognition of their outstanding work in an area of biochemistry and molecular biology. The Fellowships provide funds to assist the recipient to attend an overseas conference in a field associated with biochemistry or molecular biology, or to visit briefly a research laboratory in Australia or elsewhere to access specialised equipment or to learn new research techniques.*

Science Meets Parliament 2024

Michael Roach arrives at Parliament House, Canberra.

Science Meets Parliament (SMP) is the premier event hosted each year by Science & Technology Australia (STA). The STA is the peak body representing those of us in the science and tech industry, providing a voice to policymakers, industry and the media to advocate for a strong STEM sector. SMP is designed to facilitate engagement between those of use working in STEM and the policymakers in Canberra. The SMP program provides the foundations for engaging effectively with parliamentarians in the lead-up to the event, and the event itself is an excellent platform for connecting with policymakers, as well as media professionals and potential collaborators. SMP2024 was held in person over two days, with some online runway sessions the week prior to help delegates prepare.

Practice your pitch

The first runway session provided excellent advice and examples on delivering your pitch. This theme of effectively communicating complex scientific concepts for non-experts was a common element throughout the entire event. The session included a lot of common tips and tricks for good science communication, but the advice that stood out for me was that usage of props is usually a big hit, and to have several different elevator pitches (30 seconds, 2 minutes, 5 minutes, etc). I kept my prop simple and printed out some high-quality photos that people could keep of a recent spatial transcriptomics experiment. It was a great way to showcase the immensity of data that can be generated from a small tissue section.

Preparing to meet a parliamentarian

The second runway session covered preparing to meet a parliamentarian. Delegates attending on behalf of STA members are granted the opportunity for a meeting with a member of parliament. For many delegates, this is their first time visiting parliament house or meeting with a parliamentarian and there was a lot of practical advice (comfy shoes, don't be late, how to dress, etc) as well as how to approach the actual meeting. Again, common themes emerged in all the advice: reminding us that they are people too, to temper our expectations and that you 'get more flies with honey'.

Australia's R&D future

After catching the red-eye to Canberra on Tuesday morning, I arrived just in time for the opening keynote by Professor Emma Johnston on Securing Australia's future in a global R&D race. This talk really set the tone for the rest of the conference. Professor Johnston, in addressing the need for sustainable research funding in Australia, provided a comprehensive summary of the significant social and economic benefits of research funding throughout society. Likewise, the consequences of under funding impacts every household and this impact can last generations. Professor Johnson closed with the importance of building trust with the public for driving real change. As scientists, directly engaging with the public is difficult, but we can empower our parliamentarians and media professionals to effect such change.

No one gets to solve all the problems on their own

The STEM leadership panel, chaired by STA president Professor Sharath Sriram, featured Australia's Chief Scientist Dr Cathy Foley, CSIRO Chief Executive Professor Doug Hilton and Yawuru epidemiologist Associate Professor Kalinda Griffiths. This was an excellent Q&A platform for some of Australia's most influential science leaders to reflect on the future of the sector. Here, the importance of diversifying the Australian economy away from mining, and of maintaining our R&D discoveries, were discussed. We don't have the same level of industry investment as other countries and we need to increase those important partnerships to stay competitive. The conversation jumped to many different topics including public apathy towards science. An interesting observation was that all young kids tend to love science, so what is driving younger generations away from it?

Understanding Australia's democratic system

The Former Speaker of the House Professor Hon Tony Smith talked about the quirks of Australia's democratic system and how advice from STEM experts fits, or misses, the political agenda. Scientific advice needs to be clear and concise. It also needs to be either presented or remembered at the right time. I heard countless examples of positive legislative outcomes that occurred solely because a parliamentarian happened to recall an interesting recent conversation.

Policy advisors hate work–life balance

One of my favorite sessions was hearing about a day in the life of senior advisors. The conversation followed the experiences of Brooke Curtin (Senior Advisor, Office of the Hon Paul Fletcher MP) and Dr John Byron (Principal Policy Advisor, Office of the Vice-Chancellor, QUT). The days can be grueling, with Brooke joking that they're often ready for lunch at 9am when everyone else is starting

their day. It was interesting listening to the vastly different experiences of life in government versus opposition. Both Brooke and John had excellent advice for engaging with parliamentarians, and much of it seemed to circle back to concise and engaging science communication skills.

National Press Club Address

STA President Professor Sharath Sriram gave a stellar address at the National Press Club of Australia making the case for greater investment in science. If you have not watched it yet, I strongly suggest you do so. Professor Sriram opens with some examples of Australian inventions that are ubiquitous in society worldwide, but which Australia has not benefited from as the commercialisation occurred overseas. He gives other examples of success stories as outliers that highlight all the significant roadblocks for anyone wanting to commercialise within Australia. While other OECD economies are increasing research spending (percent of GDP), Australia is in freefall and we are being left behind. Professor Sriram concludes with a path forward and a clear mandate for Australia achieving 3% of GDP on R&D as fast as possible. Getting Australia back on track will take a sustained effort from government, industry and Australia's research institutions.

Don't give up

The key skills for science advocates followed nicely from the National Press Club address. It was very apparent by this point that everyone was intimately aware of the challenges we face, with political will being a significant hurdle for change. We heard from science advocate experts Anna-Maria Arabia (CEO Australian Academy of Science), Feyi Akindoyeni (Partner SEC Newgate) and Matthew Cossey (CEO of CropLife Australia). The common theme in this session was long-term thinking; many seemingly overnight success stories are actually years in the making. The practical advice in this session largely related to fostering mutually-beneficial long-term relationships with parliamentarians.

First Nations knowledge

In the last session on Tuesday, we heard from Professor Chris Matthews (Quandamooka mathematician, ATSIMA Chair and STA Board Director), Dr Katrina Wruck (Mabuigilaig/Goemulgal chemical engineer), Tiahni Adamson (Torres Strait Islander environmental scientist, Superstar of STEM), and Associate Professor Bradley Moggridge (Kamilaroi indigenous water scientist) on elevating first nations knowledge as a priority. We heard about the necessity of trust for building lasting connections, and the importance of protocols for engaging with communities for collaborating. I was particularly interested in what we as individuals can do to help.

Galah tastes suspiciously like chicken

The Gala Dinner was an energetic finale to the first day, with pre-dinner drinks and networking in the marble foyer. After talking to so many STEM experts from such disparate fields I found a renewed appreciation for those in parliament trying to stay up to date with current research trends. Ngambri Elder Paul Girrawah House gave a wonderful Welcome to Country at the dinner. We heard a fantastic talk from the Hon Ed Husic MP, Minister for Industry and Science, which reiterated the sentiments throughout the day and outlined the government's vision for the future. We also heard from Shadow Minister for Science the Hon Paul Fletcher MP and Dr Cathy Foley AO PSM was a crowd-pleaser. Members of parliament and senior government officials were distributed across the tables and I had a fascinating conversation with a senior official from the Treasury.

Federal Minister for Industry and Science, the Hon Ed Husic MP, speaks at the SMP Gala Dinner.

Parliamentary forum

Day 2 kicked off with a parliamentary forum with Nationals Senator Perin Davey, Liberal MP Aaron Violi, Labor MP Zaneta Mascarenhas, Greens Senator David Shoebridge, Independent Senator David Pocock and Independent MP Allegra Spender. We again heard the importance of frank and succinct communication, and of understanding the realities of the political landscape, for instance when delivering uncomfortable truths. Senator Pocock remarked that our current level of investment in science was an embarrassment. Senator Shoebridge remarked on the challenges of AI and climate. Zaneta Mascarenhas MP highlighted how flexible working for leadership positions is required for increasing women in STEM leadership roles. On the topic of how to engage there were several view: Senator Shoebridge suggested establishing a body for advice; Member Mascarenhas agreed that science needs a seat at the table; Senator Pocock promoted directly reaching out; Allegra Spender MP encouraged getting the message out to the community; Aaron Violi MP reiterated presenting your ask straight away; and Senator Davey reiterated that your message must always be 'glass half-full'.

Science Meets Parliament 2024

Science & Technology AUSTRALIA

Saving the planet

We next heard from UNSW Scientia Professor Martin Green, in conversation with Dr Cathy Foley AO PSM. In 1983, Professor Green's team developed the record-breaking technology in photovoltaics which is still used in the majority of systems today. This fascinating keynote followed the evolution of photovoltaics and their lasting positive impacts for society.

Lego Parliament House – one of many attractions inside the real, non-Lego Parliament House.

Science advice in public policy

After morning tea, we heard from Meghan Quinn PSM (Secretary, Department of Industry, Science and Resources), Tony Cook PSM (Secretary, Department of Education), Blair Comley PSM (Secretary, Department of Health and Aged Care) and Emeritus Professor Cheryl Praeger AC (National Science and Technology Council). This leadership panel encompassed understanding how advice from STEM experts fits into the framework and how best to advise senior policy makers to positively inform policy decisions. There were some interesting discussion points such as a preference for STEM experts that are politically aware but not involved in politics, and barriers to engaging such as a narrow expertise or unwillingness to discuss unpublished results. The discussion again touched on communication with policy-makers, e.g. the elevator pitch and knowing your audience. It was amusing but unsurprising to learn that policy advisors Google who the experts are (keep your profiles up to date), but reassuring to hear about the importance of advisory bodies. My takeaway message was that it's a complex landscape, with issues often involving multiple departments, but that we are encouraged to participate in such advisory bodies (including STA).

Getting science in the news

Getting the public excited about scientific achievements has never been more important. We heard from a discussion panel of Donna Lu *(Guardian Australia)*, Brandon How (InnovationAus) and Nate Byrne (ABC News Breakfast). The charismatic Nate had some excellent insights into the media landscape, including how much influence the journalists have in what gets printed, and of the importance of having a story – there's ***always*** a story. Smart people that can't communicate are very hard for broadcast, whereas excellent science communicators are often featured regularly. I highly recommend checking out innovationaus.com for a broad range of science and tech related news.

Meeting a parliamentarian

I was fortunate to be able to meet with Tasmanian Senator the Hon Richard Colbeck together with fellow ASBMB member Erin Brazel and two other talented researchers. Senator Colbeck had an impressive display of sports memorabilia and unique display pieces. We introduced ourselves and began presenting our pitches. We had a brief interruption when the Senator had to leave and vote on a piece of legislation, and this was interesting to watch on the monitors from the office. Erin Brazel presented some of the amazing work her team at GPN Vaccines are achieving. I presented some recent work on spatial transcriptomics and how this new technology will accelerate cancer research. We asked the senator what sort of science he wanted to hear about and his interests largely followed those of his constituents, for instance agriculture, forestry and fishery industries. I was able to speak to my previous work at the Australian Wine Research Institute identifying clonal markers for most of the Chardonnay and Pinot Noir clones in Australia, and the positive impact it has had on the industry. It was an interesting experience and I'd highly recommend meeting a parliamentarian if you get the chance.

From left: Cameron Gordon, Michael Roach, Senator the Hon Richard Colbeck, Caitlin Curtis and Erin Brazel.

Parliament house is a pretty cool tourist spot

I returned to catch the tail end of Professor Bryan Gaensler and Professor Brian Schmidt AC FRS FAA FTS talking about their illustrious careers in astronomy.

Science Meets Parliament 2024

Science & Technology AUSTRALIA

During the afternoon break, delegates had the option of attending question time or a number of tours. There is a lot to see in Parliament House including many incredible First Nations artwork, portraits of former PMs and even a lego Parliament House.

US Ambassador to Australia

We were privileged to hear from the US Ambassador to Australia, Caroline Kennedy. Ambassador Kennedy's speech touched on many aspects you would expect, including strengthening of the alliance under President Joe Biden, culminating relatively recently with the AUKUS security partnership. Ambassador Kennedy outlined the USA's aspirations to halve cancer deaths by 2050 with the Cancer Moonshot initiative, as well as cooperation with Australia in tackling the climate crisis. These three pillars of the alliance – defense, economy, climate and energy – are intimately linked with advancing science and technologies. The gratitude she expressed for the important work that we all do was a wonderful end to the conference.

Dr Michael Roach is a Senior Bioinformatician at SAiGENCI and is the ASBMB South Australia Representative.
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Australian Academy of Science Honour for ASBMB Members

On 3 April 2024, the Australian Academy of Science awarded twenty-two Australian researchers for their contributions to the advancement of science, including ASBMB member, Tony Weiss, who was awarded the Ian Wark Medal and Lecture.

Tony Weiss AM is the McCaughey Chair in Biochemistry, NHMRC Leadership Fellow, and Professor of Biochemistry and Molecular Biotechnology at the University of Sydney. He leads Tissue Engineering and Regenerative Medicine in the Charles Perkins Centre. His research is on the biochemistry, molecular and cell biology of the elastic extracellular matrix.

Tropoelastin is the protein building block that provides human tissue with its elasticity. Tony's work has established tropoelastin as a vital field of research in work that underpins novel applications and clinical translation in wound repair. His lab discovered how to modulate tropoelastin self-assembly and articulated the rules governing this assembly process to give elastin. He then created intricate elastin architectures tailored to elastic tissue including skin and blood vessels, where it coordinates cell growth and organised tissue repair. He has defined tropoelastin's shape and elucidated how cells respond to tropoelastin through specific integrins and their binding mechanisms.

Tony has been awarded the Prime Minister's Prize for Innovation, NSW Premier's Prize for Science and Engineering Leadership in Innovation, Eureka Prize for Innovation in Medical Research, Australian Academy of Technology and Engineering Clunies Ross Award, Australasian Society for Biomaterials and Tissue Engineering Award for Research Excellence, AMRAD Pharmacia Biotech and Lemberg Medals from the ASBMB, Barry Preston Award from the Matrix Biology Society of Australia and New Zealand (MBSANZ), FAOBMB Entrepreneurship Award, and the Applied Research and Weickhardt Medals from the Royal Australian Chemical Institute.

Tony Weiss.

Tony is President of the Tissue Engineering and Regenerative Medicine International Society (TERMIS), was elected Chair of TERMIS Asia Pacific, and President of MBSANZ, and is a Fellow of the Australian Academy of Technology and Engineering, Royal Society of NSW, Royal Australian Chemical Institute, Royal Society of Chemistry (UK), Royal Society of Biology (UK), American Institute for Medical and Biological Engineering (USA), National Academy of Inventors (USA), Tissue Engineering and Regenerative Medicine, and Biomaterials Science and Engineering. He was an NIH Fogarty International Fellow, and Fulbright Scholar at Stanford University, and has served as the NSW State Representative for ASBMB.

Tony continues to be inspired by his former PhD supervisor, Gerry Wake, and other his mentors. Tony is deeply appreciative of his extraordinary lab members and scientific collaborators who have enriched and continue to nurture his scientific journey.

ASBMB Member Elected Fellow of the Australian Academy of Science

On 23 May 2024, the Australian Academy of Science announced the election of 24 new Fellows for their outstanding contributions to science, including ASBMB member, Professor Glenn King.

Professor Glenn King works in the Institute for Molecular Bioscience at the University of Queensland. He is the leading figure worldwide in the study of arthropod venoms and the development of venom peptides from these animals as pharmacological tools, human therapeutics and bioinsecticides. He has made seminal contributions with respect to our fundamental understanding of the evolution, ecology, production and functional and structural diversity of arthropod venoms. His research investigates venoms from predators including spiders, scorpions and centipedes.

Professor King's ground-breaking research on safer ways to control disease-spreading pests and to protect crops has led to the first commercial application of venom peptides as environmentally friendly insecticides which are safe for humans and bees. He founded the company, Vestaron, which has developed safe and eco-friendly insecticides for farmers. This instigated a revolution in crop protection, helping address global food challenges.

He is co-founder and Chief Scientific Officer of Infensa Bioscience, which is developing venom-derived therapeutics to help treat strokes and heart attacks. Infensa plans to start Australian-based clinical trials for heart-related therapeutics in 2025.

Glenn King.

Glenn has been a member of ASBMB since 1982 when he attended his first scientific conference, the ASBMB meeting in Perth.

Patent Applications for Busy Academics – Why Bother?

Dr Harriet Manley (Associate) and Dr Sarah Hennebry (Associate Principal) from FPA Patent Attorneys describe the benefits of filing a patent application.

Harriet Manley (top) and Sarah Hennebry.

As registered patent attorneys, it will come as no surprise that we appreciate the value of patent protection. But for an academic researcher, is preparing and filing a patent application worth the time and effort? You're working hard gathering new data, analysing, writing manuscripts and grant applications, teaching and more – so is intellectual property (IP) just another thing to do?

In our last article, we discussed the differences between patent applications and granted patents that provide enforceable patent rights. This article outlines some of the benefits of filing a patent application – some of which may be surprising and arise long before the application is converted into a granted patent.

Preparing a patent application

Firstly, drafting of a patent application may be more straightforward than you think. If you have a draft manuscript prepared for submission, this manuscript can provide most, if not all, the information needed for a patent attorney to prepare a patent application for filing. This includes draft manuscripts prepared for uploading to preprint servers such as bioRxiv, ChemRxiv and arXiv.

The key is to file the provisional patent application **before publishing** the invention elsewhere, to establish a priority date and that the invention is novel (see our earlier articles).

Importantly, certain research institutions contractually oblige researchers/employees to share that they have a potentially patentable invention, and contemplate filing a patent application, before researchers can proceed with publishing in academic publications.

The big picture: innovation and commercialisation

As discussed in our previous article, obtaining a granted patent provides the patentee exclusive, enforceable rights to prevent others from infringing (using the invention), and the right to license or sell the patent as a revenue stream.

The *quid pro quo* of the patenting system is that once the patent application is published (approximately 18 months after filing), the public receives a detailed description of how the invention works and how to produce the invention. This contrasts with a trade secret, where confidential information is kept in-house for only those 'in the know' to use and benefit from.

There is sometimes a misconception that patent documents are secretive and prevent the collegial spread of knowledge. But because the application is ultimately published, others can build upon the knowledge within a published patent application – much like a published journal article in academic settings. Patents are therefore broadly considered to stimulate and accelerate research and development of new and innovative products, and to provide a technological and economic benefit for society.

Even if you are not entrepreneurially minded, investigating and beginning the patent protection pathway is the first step for commercialising an idea. A patent application provides a platform to maximise the real-world impact of your scientific research by enabling the translation of an idea into a commercial product – for example, a pharmaceutical that helps patients.

Without IP protection, your scientific research may not attract investment or be further developed by industry (e.g. biopharmaceutical companies, venture capital groups). This is because an absence of patent filings (and reliance solely on trade secrets) is often perceived by industry parties as extremely high-risk. The monopoly obtained by patent protection is a mechanism by which industry parties achieve commercial compensation for any time and money they've invested into R&D. Without a patent filing, there is no opportunity for this monopoly, and instead increased risk of competition.

Patent Applications for Busy Academics – Why Bother?

Funding opportunities

Research grants

IP is increasingly impacting research grants and becoming a metric used in grant applications to assist researchers in securing funding.

For example, the National Health Medical Research Council (NHMRC) directs peer-reviewers to consider 'industry-relevant experience' (1) when assessing grant applicants (e.g. for Ideas and Investigator Grants). This includes recognition for non-traditional research outputs such as patents and patent applications, industry collaborations and commercial agreements (e.g. research services, material transfer, licensing agreements).

Notably, NHMRC Peer Review Guidelines also explicitly include consideration for when an academic publication is delayed due to patenting (1). This may assure grant applicants that taking the time to file a provisional application first, before publishing the related journal article, is unlikely to harm grant prospects (whereas this approach will significantly improve patenting prospects).

Several grant schemes also prioritise translational and/or clinical research including the Medical Research Future Fund (MRFF) (2), JDRF clinical trial proposals (3), NHMRC Clinical Trials and Cohort Studies Grants (4) and Support for Cancer Clinical Trials Program from Cancer Australia (5). These schemes often ask applicants to outline the commercial significance of the proposed research, including whether research will lead to commercial research outputs (including patents) and industry partnerships. Already having filed a patent application or indicating potential generation of commercially valuable IP, can be useful to incorporate into applications for translation-focussed schemes.

Early-stage commercialisation grants

Early-stage commercialisation grant programs can require submission of an IP plan and/or evidence of ownership/control over the IP when applying (6,7). Such programs can be targeted towards small to medium entities and entrepreneurs rather than academic researchers but are still worthwhile to consider.

Filing a provisional application, standard Australian patent application and/or international PCT application are all steps that assist a funding strategy relying upon these types of grants, because they help demonstrate an existing IP strategy and intention to commercialise. Further, obtaining early opinions of patentability (i.e. the likelihood of the patent application becoming a granted patent) can strengthen a grant application (8).

Industry funding

Research funding can also be obtained via industry partnerships. As discussed above, IP helps attract investor funding as it helps de-risk investments. Patent filings and positive patentability opinions are valuable indicators for industry investors that the research could be successfully commercialised.

Industry funding can arise from:

- Angel investors (usually individuals who invest their own money in exchange for a minority stake in the start-up company or business. Angel investors may also provide mentorship).
- Venture capital (VC) funds (private investors that provide capital generally to support start-ups and early-stages businesses with potential for rapid growth, in exchange for an equity stake). VC groups can include those with government backing, such as Breakthrough Victoria (9).
- Licensing agreements with pharmaceutical companies.

It may surprise some readers that funding from industry partners can be obtained at proof-of-concept or preclinical research stages (10,11,12,13), and is **not** restricted to later clinical trial phases. In addition to funding, angel or VC investors can sometimes also provide valuable mentorship and other assistance along the commercialisation pathway (e.g. networking, operational help, research spaces).

Programs run by non-profit organisations, such as the Heart Foundation (14), or by industry incubators, such as Jumar Bioincubator (15) and CUREator from Brandon Biocatalyst (16), can help connect researchers with interested investors.

Caveats to IP and funding

Disclosure

When applying for grants, there is an expectation of confidentiality between the grant applicant and the reviewing body. However, this should be assessed before putting commercially sensitive information into a grant application. Non-confidential disclosure of your invention can jeopardise your ability to patent, because to be patentable, an invention must be new/novel.

Similarly, it is crucial to ensure that you do not disclose your invention to a third party (e.g. potential industry investor) without having appropriate confidentiality agreements in place. Preferably, a patent application for your invention is filed before initiating discussions with industry partners.

Conditions

Funding agreements often have clauses or requirements for how IP generated under the funding scheme is handled. Research contract clauses are commonplace but do warrant consideration by those undertaking the funding agreement. As with funding schemes, investors can also place conditions on how their investment and generated IP are used. As with research grants requesting reports

Patent Applications for Busy Academics – Why Bother?

of research progress, industry investors may require reports of achieving specific research and/or commercial milestones.

Industry agreements

Patent filings can serve as useful tools to delineate who owns particular IP when entering into agreements (e.g. licensing deals, research collaborations) with third parties. This is particularly important for researchers to consider when they wish to provide research services to a third party where the services may involve their IP or generating new IP by using a product licensed from a pharmaceutical company (e.g. an antibody or drug compound). As patent attorneys, we do not advise on the terms of such legal agreements (that is the realm for IP lawyers) but do recommend filing patent applications where appropriate as they can assist navigating these situations.

Costs

Applying for a patent application incurs some costs, so it can appear counteractive to pursue a patent application whilst trying to raise money for research. It can also appear counteractive to file a patent application, which is initially non-published, when you are trying to disseminate your research findings.

However, research institutions and universities can enable the patenting process whilst helping you achieve your research goals. If you are interested in patenting a scientific invention, we recommend that you reach out to your technology transfer office as well as your friendly patent attorney.

Take-home messages

- The patenting process drives innovation and commercialisation, helping scientific research have real-world impact.
- Filing a patent application can facilitate research funding via grant schemes and opens up new funding opportunities from industry investors.
- Having a patent application or patent directed to your IP protects against inadvertent self-disclosure of the invention when having discussions with third parties, e.g. industry partners. Alternatively, another way to protect from self-disclosure is ensuring proper confidentiality agreements are in place before entering into commercial discussions.
- IP generated using grant or industry funding can come with its own caveats, but filing a patent application can help clarify who owns what if there are commercial agreements to be made.

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ASBMB Fellowship Report

Gut Feelings and Windy City: Navigating Chicago and Intestinal Cancer

Chicago, the bustling hub of commerce and culture, hosted a pivotal event in the realm of medical science – IMMUNOLOGY2024™, a conference organised by the American Association of Immunologists in May 2024. I am grateful to have received an ASBMB Fellowship that supported my trip to this conference where I presented my research on DNA sensors and their implications in intestinal cancer. Cancer is a global health burden, with the incidence of bowel cancer expected to increase by 63.6% globally and by 51.4% in Australia in the next 20 years. Research into harnessing the power of our immune system in the treatment of cancer could help achieve the important goal of preventing cancer-related deaths.

A key component of medical science research is collaboration and interaction with colleagues from around the world who work in the disciplines of biochemistry, molecular biology and immunology. Therefore, attending conferences and scientific meetings is critical to research. The American Association of Immunologists has been the world's leading forum for researchers dedicated to advancing the field of immunology through the elucidation of the principles of immune function. This meeting brings together a wide range of scientists incorporating disciplines across biochemical and molecular modulation of immune signalling pathways in humans and animals.

One of the most transformative experiences I had during this conference was the roundtable careers sessions. I was intrigued to hear about the challenges faced by researchers in establishing and running independent research groups. I expect the advice, suggestions and comments from these sessions will guide me on my path towards independence. In addition, I had a unique opportunity to explore the latest technical developments in immunology. I learned about new techniques for gene and protein modifications and advances in the field of high-resolution microscopy and spatial biology.

Abhimanu Pandey.

Despite my struggle with jetlag, I presented my poster, a visual encapsulation of my research. Engaging in discussions with fellow researchers, I gained fresh insights and perspectives, enriching my understanding of the intricate nuances surrounding DNA sensors and intestinal health. The following day, I ascended the podium to deliver my presentation on the role of DNA sensors in intestinal cancer. I was enlightened by the diverse perspectives and novel insights shared by my peers during and after my talk.

Networking emerged as an integral aspect of this conference, offering a gateway to forge meaningful connections and collaborations. From casual conversations over coffee to engaging discussions during poster sessions, I interacted with researchers from around the world. These interactions not only broadened my professional network but also sparked new avenues of inquiry and exploration, laying the foundation for potential collaborations and partnerships in the future. Beyond the confines of the conference hall, I experienced the city's vibrant charm and allure. My journey to Chicago for this conference proved to be transformative, fuelling my passion for scientific inquiry and discovery. I'm sincerely grateful to the ASBMB for providing me the opportunity to attend a fantastic meeting!

Dr Abhimanu Pandey is a postdoctoral researcher at the John Curtin School of Medical Research at the Australian National University.

ASBMB Welcomes New Members

A warm welcome is extended to the following new members who joined ASBMB from 1 July 2023 to 30 June 2024

ACT
DR VICKI ATHANASOPOULOS
PROF STEFAN BROER
A/PROF MARIAN BURR
DR KAI XUN CHAN
DR JOHN CHEN
PROF IAN COCKBURN
MS ALEXANDRA CORAM
MR JACK DALTON
DR FLORENCE DANILA
MISS LANI DAVIES
MISS ASMITA DEONATH
MR TIRATH DWIVEDI
MISS RUISI FAN
DR RITA FERREIRA
MR BARNABAS GALL
MR ANDY GARCIA
MISS ROSEMARY GEORGELIN
MISS CHLOE GOMEZ
MISS VRINDA GUPTA
DR NADINE HEIN
MS EVIE HODGSON
MS SHAGUFTA IQBAL
MR RUIZ FLORES JESUS
DR RUITAO JIN
DR PETER JOHNSON
MISS NIVEA KAKDE
MR HYUNJIN KIM
DR JOACHIM LARSEN
MRS ZHAO LI
MS YC LIN
MISS JIANSI LONG
DR COLLEEN MACMILLAN
DR SAMANTHA MCGAUGHEY
A/PROF TONY MILLAR
MR VISHNU MINI SASI
MS AMINA MUSTAFA
A/PROF RICCARDO NATOLI
A/PROF CHRISTOPH NITSCHE
DR ABHIMANU PANDEY
DR KAPIL PATEL
PROF ADAM PERRIMAN
DR ROSA PRAHL
DR HAOCHENG QIANZHU
DR MUNAZZA RAJPUT
DR RACHAEL REMINGTON
MR JESUS RUIZ FLORES
MISS PAREMILA SHANMUGA NATHAN
DR MARK SHANNON
DR NAVNEET SINGH
MR OLIVER SMITH
MS ALEXANDRA SNEDDON
MR JOHN TANNER
MS ELAINE TAO
MISS NUREN TASNEEM
DR ERICK TJHIN
MISS HELANA TRANTINO
PROF DAVID TSCHARKE
MS CYNTHIA TURNBULL
PROF NARESH VERMA
MISS CIARA WALLIS
DR RACHEL WOODHOUSE
MS SUYAN YEE
MS SKYE YOUNG
MISS XIAOJUN YUAN
MS JING ZHANG
DR BINI ZHOU

NSW
MISS SABA ALTAF
MR EHSAN ALVANDI
MS ALLEGRA ANGELONI
A/PROF MATTHEW BAKER
MS HANNAH BROWN
PROF MIN CHEN
DR OSVALDO CONTRERAS
MISS ANDREA DANERS
DR JENNILEE DAVIDSON
MRS JULIANNA LYS DE SOUSA ALVES NERI
DR ALEXIS DIAZ VEGAS
MS SARA ESMAEILI
MISS ZAHRA FALAHATI
DR OLIVER FULLER
MS SONIA GOOZEE
DR JODY GORMAN
MS MIA GRUZIN
MR JYOTI GURUNG
DR JOSHUA HAMEY
DR DOAA HANAFY
MISS GEMMA HART
MS LISSY HARTMANN
MR ALFRED HARTOJO
MS MIKAYLA HOAD
MS XIAOJING HUANG
MISS JIALI HUANG
MISS XUEFEI JING
DR CAITLIN JOHNSTON
MISS NICOLA KARAKATSANIS
MR EREKLE KOBAKHIDZE
MR LUCIEN LAMBRECHTS
DR JACOB LEWIS
DR LANA LY
DR NICHOLAS MARZANO
DR STEWART MASSON
MS THILINI MUNASINGHE
MISS JASMINE MINH HANG NGUYEN
MR JORDAN NICHOLLS
DR MARTIN PAL
DR ASHLEIGH PAPARELLA
DR GAYLE PETERSEN
MS NATALIA PINELLO
MISS ANASTASIYA POTAPENKO
MISS ANASTASIYA POTAPENKO
MS ANNALISE PSAILA
MS SHANON RANJIT
MR DANIEL REED
DR PIETRO RIDONE
DR MANAN SHAH
MRS VINAYA SHINDE
DR DAISY SHU
DR REECE SOPHOCLEOUS
MR ANDREW SPITERI
MISS SOPHIE WACHER
MS EMILY WAGON
MR LIHUA YANG
PROF HAIBO YU
MR MINGCHANG ZHANG
DR YICHEN ZHONG
MR JACKIE ZHOU
DR ZIJING ZHOU

QLD
MR DESYE MISGANAW AMBAW
MR NICOLAU BARBOSA PALMA FILHO
DR FARRAH BLADES
DR ROSEMARY CATER
A/PROF MARLOES DEKKER NITERT
DR ELENA EREMEEVA
MS RACHAEL GOODY
DR YOSEPHINE GUMULYA
MRS QIAN GUO
PROF GLENN KING
DR LENNART KUCK
MISS YASMINE LAM
MS SWAGATA MUKHERJEE
DR YOOCHAN MYUNG
DR PAVLINA NAYDENOVA
MISS TIARNA RILEY
MR FORHAD SAIKOT
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MISS TEA KNEZEVIC
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MISS YUEN TUNG NGAI
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PROF VADIM SUMBAYEV

Election of Council 2025

Nominations are called for the following positions on the Council of the Australian Society for Biochemistry and Molecular Biology Inc for 2025: President Elect, Secretary, Treasurer, Editor, Education Representative, FAOBMB Representative, Secretary for Sustaining Members and State Representatives.

Eligible for re-election
§ Position open

The ASBMB Council for the period 1 January 2024 to 31 December 2024 is composed of the following members:	President	R Hannan
	President Elect	M Maher
	Secretary	D Ng #
	Treasurer	K Quinlan §
	Editor	T Soares da Costa #
	Education Representative	T Kuit #
	FAOBMB Representative	M Kvansakul #
	Secretary for Sustaining Members	S Parsons
Representatives for:	ACT	C Suraweera #
	NSW	T Christie #
	QLD	C Wang #
	SA	M Roach #
	TAS	A Holloway #
	VIC	S Stewart #
	WA	A Van Dreumel §

Nomination forms are available on the ASBMB website and are to be submitted online: https://www.asbmb.org.au/asbmb/council-nomination/Site/Register. Nominations for all vacant positions must be signed and seconded by members of the Society. The nominations must be signed by the nominee to indicate his/her willingness to stand. If more than one nomination is received for any position, a ballot will be held at the Annual General Meeting. All members will be notified of any elections and members not attending the Annual General Meeting may submit a proxy form available from the Secretary.

NOMINATIONS MUST REACH THE SECRETARY BY 5PM 11 SEPTEMBER 2024
(PRIOR TO THE ANNUAL GENERAL MEETING TO BE HELD ON 25 SEPTEMBER 2024).

Annual General Meeting of the Australian Society for Biochemistry and Molecular Biology Inc.

The 68th Annual General Meeting of the Australian Society for Biochemistry and Molecular Biology Inc. will be held on Wednesday 25 September 2024 at 1710 hours Australian Eastern Standard Time. The meeting will be conducted at the Melbourne Convention and Exhibition Centre (refer to the program during the meeting for the room).

AGENDA

1. Apologies
2. Confirmation of the Minutes of Annual General Meeting No. 67
3. President's Report
4. Treasurer's Report
5. Fees for 2025
6. Elections to Council
7. ASBMB Awards 2025
8. Amendments to Constitution and By-laws
9. Any Other Business

Dominic Ng
Secretary, ASBMB

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For further information, please contact Pete Davis pdavis@atascientific.com.au 0417 778 971.

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ASBMB Council 2024

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