Thursday, 31 July 2025

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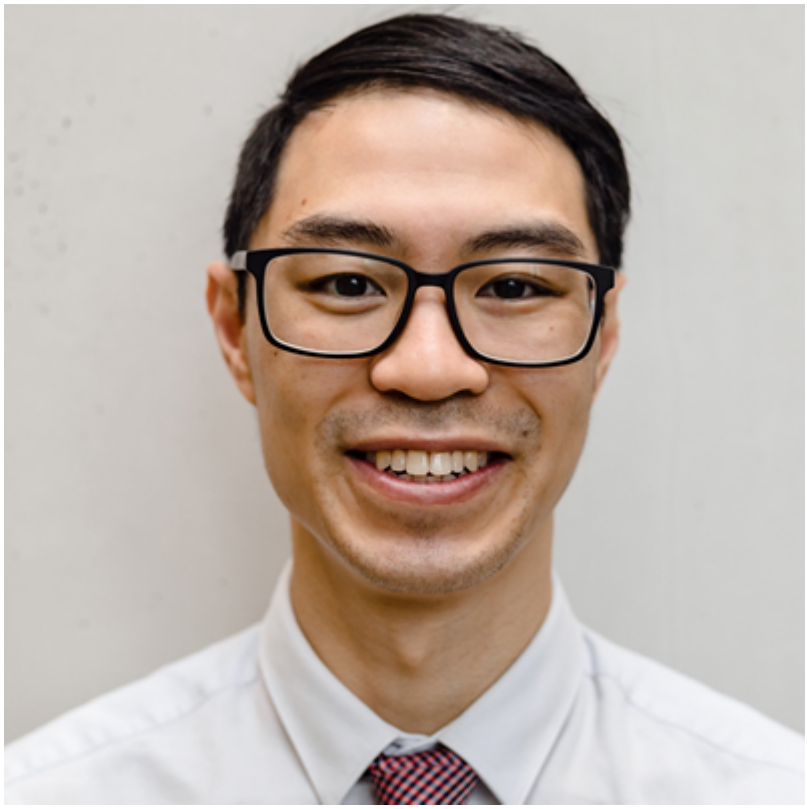
Australasian Cell Death Society

ACDS Professional Development Award 2025 winner: Dr. Adrian Lee



It is our pleasure to announce that **Dr. Adrian Lee** is the the winner of this year's ACDS Professional Development Award 2025. Dr. Adrian Lee is a Clinical Immunologist and PhD student at the Westmead Institute for Medical Research in Sydney. His research focuses on the contribution of apoptotic bodies to pathology in Sjögren's disease (SjD), one of the most common autoimmune diseases in Australia. Huge congratulations!!!

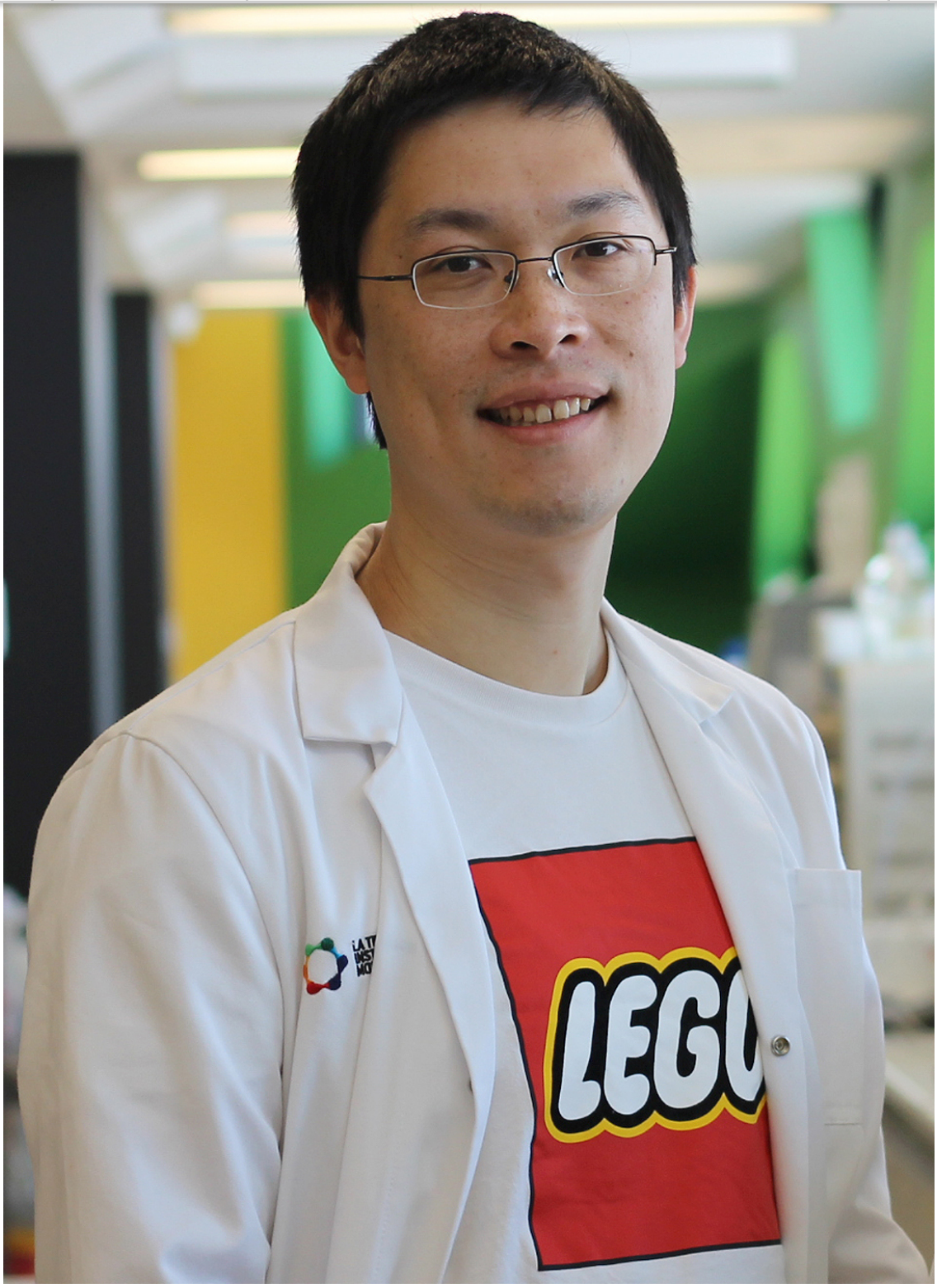
ACDS Mentorship Program - Rapid Fire Workshop Series

We are excited to have **Prof. Ivan Poon** who will be presenting in the upcoming workshop on **August 13th, 2025**.

🔷 **Workshop 3: Research Financing & Budgeting – Prof. Ivan Poon, La Trobe Institute for Molecular Science**
📅 **Wednesday, August 13th**
🕘 **2:00–2:30 AM AEDT**

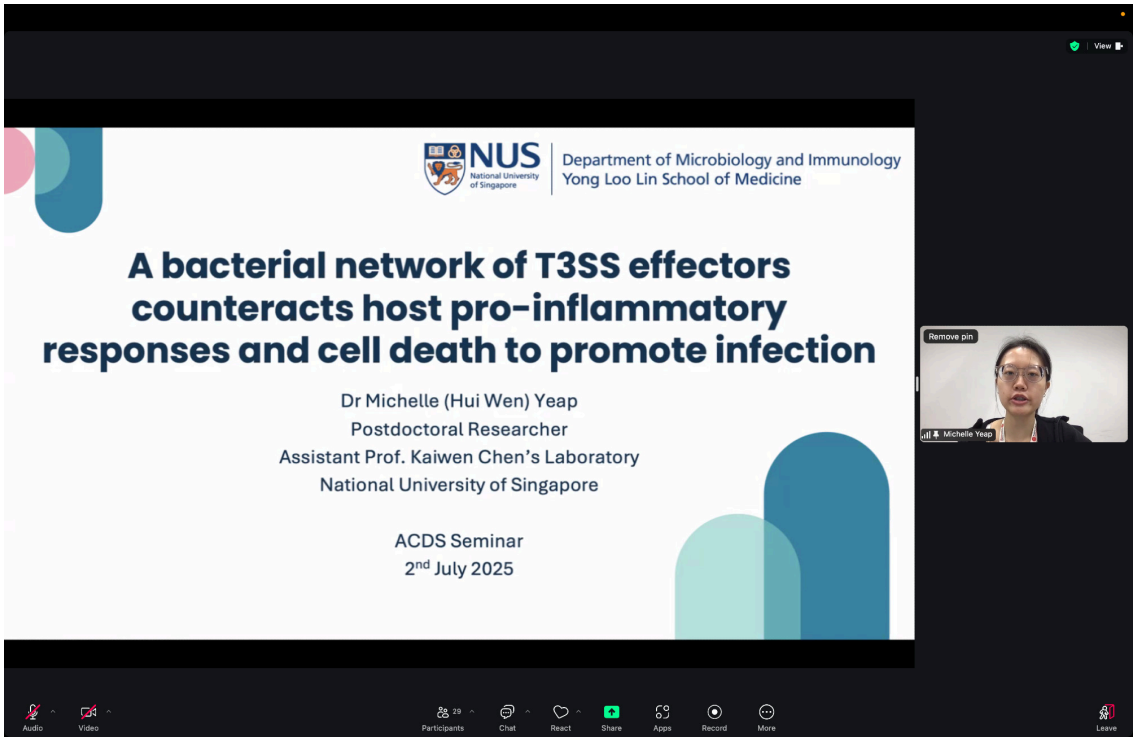
Unlock the essentials of effective financial management in research with Prof. Ivan Poon. Critical aspects in this session will cover: (1) How do you write a budget when applying for grants (i.e. lab supplies, your salaries and PhD stipend/RA salaries). (2) You've finally got a grant, how do you manage this and keep track of spending.

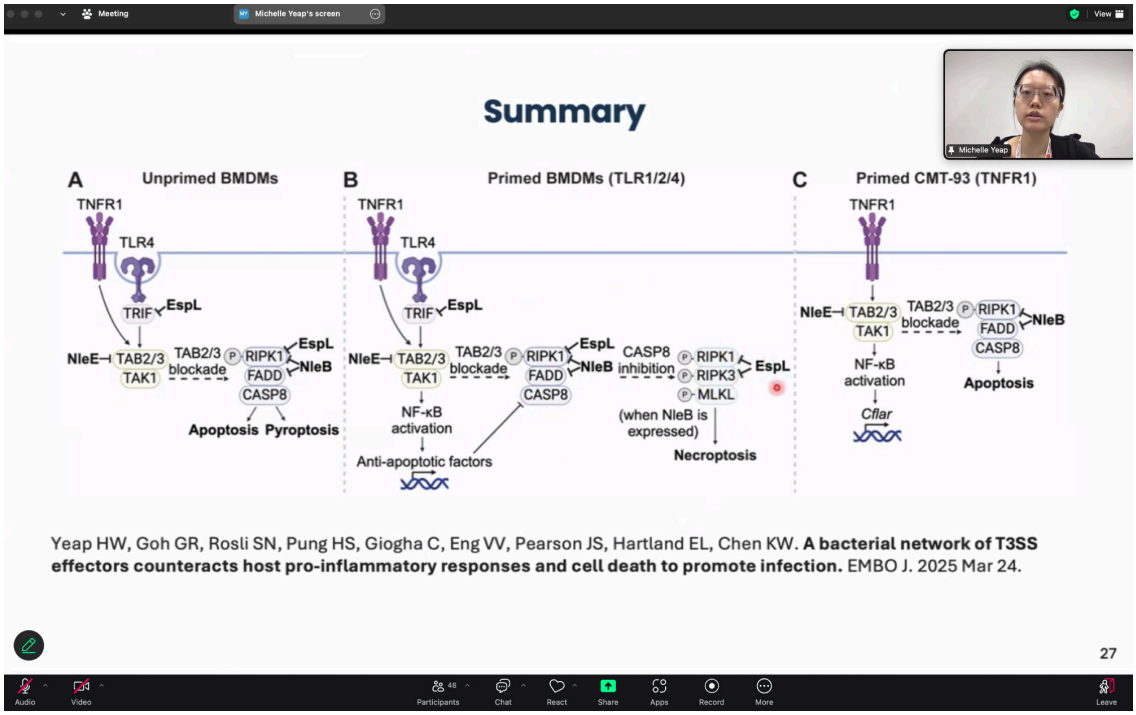
[This event is exclusive for members who have signed up for the Mentorship Programme]



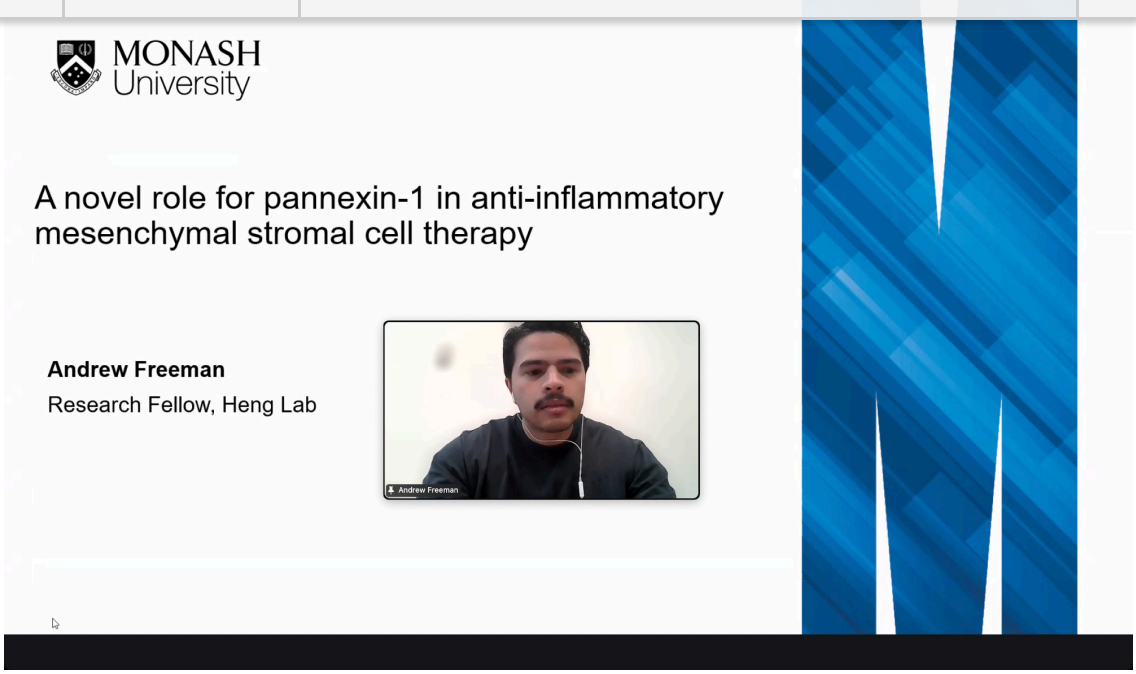
ACDS Seminar Series

Earlier this month we had two outstanding speakers, **Dr. Michelle Yeap** (National University of Singapore) and **Dr. Andrew Freeman** (Monash Biomedicine Discovery Institute) who presented their latest research in the ACDS Seminar Series.

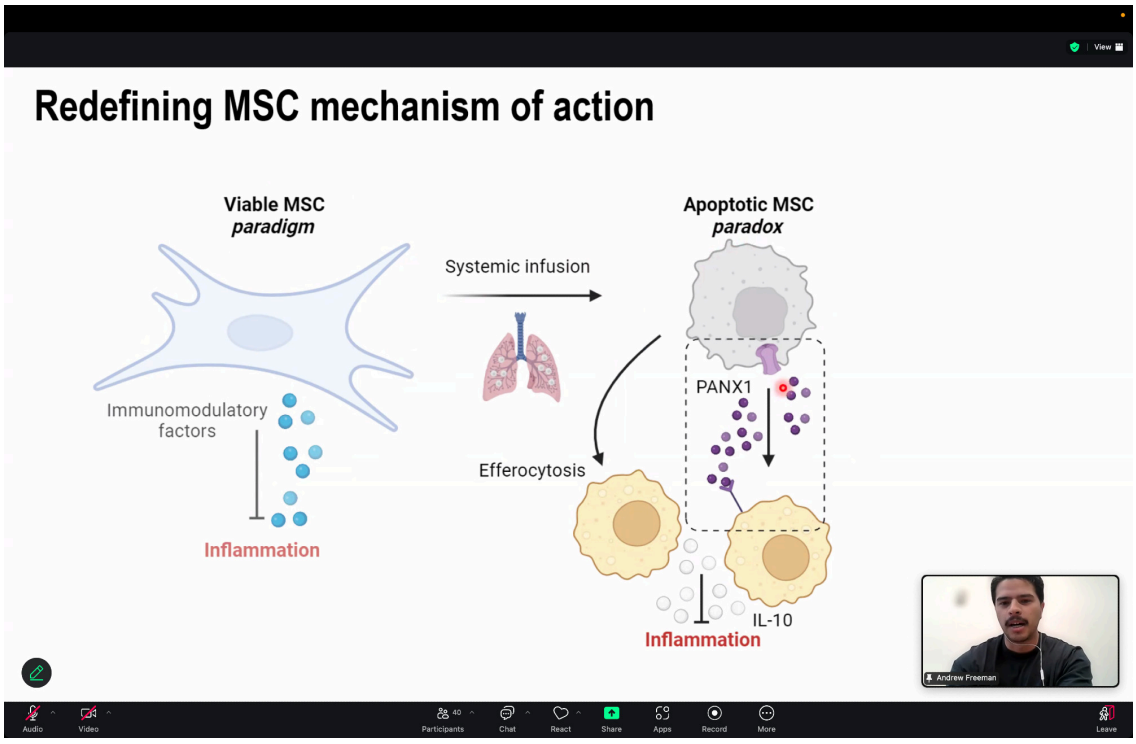




Dr. Michelle shared with us her findings on the intricate network of bacterial effectors that reshape host cell death signalling and innate immune response. Check out her latest publication here.



Our second speaker Dr. Andrew presented his insights on messenchymal stromal cell biology and the potential of pannexin-1 as a target in modulating apoptosis and inflammation.



Want to keep up to date with the latest in cell death research both nationally and internationally? Don't miss the next **ACDS x ECDO International Seminar** which will be held on **Wednesday, 13th September**. Stay tuned for more details to come!

Featured Scientist: Dr. Kerstin Brinkmann

Getting to know Kerstin

I am a Victorian Cancer Agency Mid-Career Research Fellow in the Blood Cells

and Blood Cancer Division at WEHI, Melbourne, where I lead a research program investigating the essential roles of pro-survival BCL-2 family proteins in inhibiting cell death and regulating metabolism. My work focuses on how proteins such as MCL-1 and BCL-XL control both apoptotic and non-apoptotic functions in cancer, development, and tissue homeostasis. I have shown that these dual roles operate not only in cell lines but also in vivo using gene-modified mouse models. A recent highlight is my first and corresponding author paper in *Science* (2025), which resolved a key debate by demonstrating MCL-1's essential role in mitochondrial metabolism in vivo. This underpins broader efforts to understand context-dependent BCL-2 functions and improve cancer therapies by refining the use of BH3 mimetics and identifying treatment-related toxicities.

I joined WEHI in 2015 with a prestigious Mildred-Scheel Fellowship and have since led several independent projects, producing six first-author and 14 co-authored publications, and securing over AUD 1.7 million in competitive funding as chief investigator. My reputation is reflected in over 20 invited or selected talks over the last 5 years, editorial board appointments (*FEBS* and *Frontiers in Cell Death)*, and my role as Chair of the 2024 Gordon Research Seminar on Cell Death. I currently lead a team of two PhD students and two research technicians.

Three most significant publications

1. **Brinkmann K.***, McArthur K, Malelang S, Gibson L, Tee A, Elahee Doomun SN, Rowe CL, Arandjelovic P, Marchingo JM, D'Silva D, Bachem A, Monard S, Lauren G Whelan LG, Dewson G, Putoczki TL, Bouillet P, Fu NY, Brown KK, Kueh AJ, Wimmer VC, Herold MJ†, Thomas T†, Voss AK†, Strasser A* **(2025, *corresponding author)** "Relative importance of MCL-1's Anti-Apoptotic versus Non-Apoptotic Functions in vivo" **Science** (epub ahead or press) **(first and corresponding author)**
In this 2025 Science study, I led the development and application of novel gene-swap mouse models to dissect MCL-1's anti-apoptotic function from its role in mitochondrial metabolism. With my team, I replaced the endogenous Mcl-1 gene with other pro-survival BCL-2 family members (Bcl-2, Bcl-xL, A1) to investigate whether these proteins could compensate for MCL-1 loss during embryonic development and postnatal life. While several replacements rescued early embryonic lethality, only Mcl-1^Bcl-xL/Bcl-xL mice survived beyond birth—though they exhibited severe metabolic defects. This provided the first in vivo evidence that MCL-1 is essential for mitochondrial energy metabolism and dynamics, independent of its role in apoptosis. Our findings settled a long-standing question in the field and established a new conceptual framework for understanding the overlapping and distinct functions of pro-survival BCL-2

proteins. This work now underpins a broader research program I lead within the Strasser lab, exploring how the context-specific functions of BCL-2 proteins influence development, tissue homeostasis, immune cell biology, cancer progression, and therapeutic response.

2. **Brinkmann, K***., P. Waring, S. P. Glaser, V. Wimmer, D. L. Cottle, M. S. Tham, D. Nhu, L. Whitehead, A. R. Delbridge, G. Lessene, I. M. Smyth, M. J. Herold, G. L. Kelly, S. Grabow and A. Strasser* (2020). **(*corresponding author)** "BCL-XL exerts a protective role against anemia caused by radiation-induced kidney damage." **EMBO J** 39(24): e105561 **(first author and corresponding author)**
In this EMBO Journal study, I led a project that uncovered a critical, previously unrecognised role for BCL-XL in renal epithelial cell survival. Using a novel mouse model that I developed with my team, we enabled selective deletion of BCL-XL in non-haematopoietic tissues. This approach revealed that BCL-XL is essential for kidney integrity, particularly under genotoxic stress, where its loss caused kidney failure and secondary anaemia. These findings provide important insight into the on-target toxicity of BCL-XL inhibitors and emphasise the need to account for tissue-specific functions when combining such inhibitors with DNA-damaging agents in cancer therapy.

3. **Brinkmann, K.**, S. Grabow, C. D. Hyland, C. E. Teh, W. S. Alexander, M. J. Herold and A. Strasser (2017). "The combination of reduced MCL-1 and standard chemotherapeutics is tolerable in mice." **Cell Death Differ** 24(12): 2032-2043.
In this 2017 Cell Death & Differentiation study, I led a pre-clinical investigation into the safety and tolerability of targeting MCL-1 in combination with standard chemotherapies. Using sophisticated in vivo mouse models, my team and I demonstrated that partial reduction of MCL-1 (~50%) is well-tolerated, even when combined with DNA-damaging agents. This was among the first in vivo studies to provide evidence for a potential therapeutic window for MCL-1 inhibition in cancer treatment. This work laid important groundwork for the continued development of MCL-1 inhibitors that aim to minimise toxicity while preserving anti-tumour efficacy.

We asked Kerstin a few questions about her research career

What motivates you to get into the lab?
What motivates me to get into the lab every day is my natural curiosity and love for discovery. I genuinely enjoy asking questions and digging into the unknown —that moment when a new experiment sheds light on a puzzle is what drives me. Being surrounded by a curious and driven team makes the work fun and energising. That environment helps keep me motivated even when experiments

don't go as planned, because there's always something new to learn or try next. Science is all about exploring and solving questions together, and having a great team to share ideas and tackle challenges with is incredibly rewarding. Ultimately, it's the combination of curiosity, collaboration, and the chance to contribute new knowledge that gets me excited to come to the lab every day.

What decisions made the biggest impact or have proved to be the most beneficial for your career, and what advice would you give to up-and-coming cell death researchers?

One of the best decisions I made was moving from Germany to WEHI in Melbourne to join Andreas Strasser and his team, a world-class lab focused on cell death. It was a big step, but it gave me the chance to work with inspiring people, build strong collaborations, and develop the in vivo models that now form the backbone of my research.

Being actively involved — mentoring students, helping organise conferences, joining postdoc committees — kept me in the middle of things and helped me build a strong network within and beyond my institute. I'd encourage others to do the same. You learn a lot, make great connections, and it really helps shape your path.

Networking has also been a big part of shaping my career. Putting myself out there at international conferences and approaching people I admired — even the "big names" — felt outside my comfort zone at first, but it made a huge difference. Some of the most important opportunities I've had started from a simple chat after a talk, at a poster, or over coffee. My advice: don't be shy. Most senior researchers are more approachable than they seem and are genuinely happy to support the next generation. Stay curious, stay connected, and back yourself.

What is your favourite cell death-related molecule and why?

My favourite cell death molecule has to be MCL-1. It's like the ultimate multitasker in the cell — not only does it keep cells alive when things get tough (even more than its cousins in the BCL-2 family), but it also moonlights as a key player in managing the cell's energy, kind of like a secret chef making sure the cell's "kitchen" runs smoothly. What really fascinates me is how important MCL-1 is for survival across different tissues and stages of life — it's like that one friend who always shows up and saves the day. Plus, because it's so crucial, MCL-1 is a hot target for cancer therapy. I genuinely believe that cracking the code on what exactly this molecule does will lead to better, safer treatments that could help millions of cancer patients in the future. It's a real game-changer in how we understand the balance between life and death in cells, and that's why I'm hooked on MCL-1.

What do you enjoy doing for fun or in your spare time?

In my spare time, I love staying active and spending plenty of time outdoors with my dog. Whether it's going for long walks, camping, or hitting the road in my van for a road trip, being in nature really helps me recharge. I also enjoy aerial silks, which challenge me to push past my fear of heights and step outside my comfort zone — making it both a rewarding and fun way to combine sport and creativity. But it's not all adventure—I really value quiet nights with friends and family, sharing good food and a nice glass of wine. It's the perfect balance between active days and relaxing moments that keeps me refreshed and ready for whatever comes next.

ACDS Member Publications

Published a cell death paper recently? Let us know and we'll list it here

Yeap HW, Goh GR, Rosli SN, Pung HS, **Giogha C**, **Eng VV**, **Pearson JS**, **Hartland EL**, **Chen KW**. A bacterial network of T3SS effectors counteracts host pro-inflammatory responses and cell death to promote infection. EMBO J. 2025 May;44(9):2424-2445. doi: 10.1038/s44318-025-00412-5. Epub 2025 Mar 24. PMID: 40128366; PMCID: PMC12048508.

M Bader S, **Scherer L**, Schaefer J, Cooney JP, Mackiewicz L, Dayton M, Georgy SR, Davidson KC, Allison CC, **Herold MJ**, **Strasser A**, Pellegrini M, **Doerflinger M**. IL-1β drives SARS-CoV-2-induced disease independently of the inflammasome and pyroptosis signalling. Cell Death Differ. 2025 Jul;32(7):1353-1366. doi: 10.1038/s41418-025-01459-x. Epub 2025 Feb 28. PMID: 40016339; PMCID: PMC12284219.

Pizzuto M, **Monteleone M**, **Burgener SS**, Began J, Kurera M, **Chia JR**, Frampton E, Crawford J, Oliveira M, **Kenney KM**, **Coombs JR**, Yamamoto M, **Man SM**, Broz P, **Pelegrin P**, **Schroder K**. Cardiolipin inhibits the non-canonical inflammasome by preventing LPS binding to caspase-4/11. EMBO J. 2025 Jul 16. doi: 10.1038/s44318-025-00507-z. Epub ahead of print. PMID: 40670771.

Brinkmann K, **McArthur K**, Malelang S, Gibson L, Tee A, Elahee Doomun SN, Rowe CL, Arandjelovic P, **Marchingo JM**, D'Silva D, **Bachem A**, Monard S, Whelan LG, **Dewson G**, Putoczki TL, Bouillet P, Fu NY, Brown KK, Kueh AJ, Wimmer VC, **Herold MJ**, Thomas T, Voss AK, **Strasser A**. Relative importance of the anti-apoptotic versus apoptosis-unrelated functions of MCL-1 in vivo. Science. 2025 Jul 3:eadw1836. doi: 10.1126/science.adw1836. Epub ahead of print. PMID: 40608895.

Cooney JP, Hirons A, Jansz N, Allison CC, Hickey P, **Teh CE**, Tan T, Dagley LF, Yousef J, Yurick D, Khoury G, **Preston SP**, Arandjelovic P, Davidson KC, Williams LJ, **Bader SM**, **Wang L**, **Bhandari R**, Mackiewicz L, Dayton M, Clow W, Faulkner GJ, **Gray DH**, Einsiedel L, Purcell DFJ, **Doerflinger M**, Pellegrini M. Combination antiretroviral therapy and MCL-1 inhibition mitigate HTLV-1 infection in vivo. Cell. 2025 Jul 1:S0092-8674(25)00689-0. doi: 10.1016/j.cell.2025.06.023. Epub ahead of print. PMID: 40645177.

Shojaee F, Azadian E, Wong MX, Ma X, Rickard J, **Pang J**, Hall C, Kueh AJ, **Masters SL**, Rioja I, Prinjha RK, **Doerflinger M**, **Lawlor KE**, Rashidi M, **Vince JE**. NLRP3 inflammasome-driven hemophagocytic lymphohistiocytosis occurs independent of IL-1β and IL-18 and is targetable by BET inhibitors. Sci Adv. 2025 Jul 11;11(28):eadv0079. doi: 10.1126/sciadv.adv0079. Epub 2025 Jul 9. PMID: 40632844; PMCID: PMC12239941.

Manning JA, Jesudason S, Moretti PAB, Pitson SM, Chou ASY, Shabbar M, Saad S, Pollock C,

Kumar S. Nedd4-2 ablation in kidney improves glycaemic control in diabetic mice. Cell Death Dis. 2025 Jul 5;16(1):496. doi: 10.1038/s41419-025-07826-3. PMID: 40617804; PMCID: PMC12228766.

Cao Le A, Oudin V, Dick J, Alikhan MA, **Gottschalk TA**, Lu L, **Lawlor KE**, Koo Yuk Cheong D, Mandwie M, Alexander IE, Kitching AR, Gan PY, Logan GJ, **O'Sullivan KM**. Gene therapy enhances deoxyribonuclease I treatment in anti-myeloperoxidase glomerulonephritis. JCI Insight. 2025 Jul 8:e188951. doi: 10.1172/jci.insight.188951. Epub ahead of print. PMID: 40632882.

Derde L, Gordon AC, Mouncey PR, Al-Beidh F, Rowan KM, Nichol AD, Arabi YM, Annane D, Beane A, Beasley R, Bonten MJM, Bradbury CA, Brunkhorst FM, Buzgau A, Buxton M, Cheng AC, Cooper N, Cove M, Cremer OL, Detry MA, Duffy EJ, Estcourt LJ, Fitzgerald M, Galea J, Goossens H, Haniffa R, Hills TE, **Huang DT**, Ichihara N, King A, Lamontagne F, Lawler PR, Leavis HL, Lewis RJ, Litton E, Marshall JC, Mayr FB, McAuley DF, McGlothlin A, McGuinness SP, McVerry BJ, Morpeth SC, Murthy S, Netea MG, Ogungbenro K, Orr K, Parke RL, Parker JC, Patanwala AE, Pettila V, Reyes LF, Saito H, Santos MS, Saunders CT, Seymour CW, Shankar-Hari M, Sligl WI, Turgeon AF, Turner AM, Tong SYC, Vaara S, Youngstein T, Zarychanski R, Green C, Higgins AM, McArthur CJ, Berry LR, Lorenzi E, Berry S, Webb SA, Angus DC, van de Veerdonk FL. Tocilizumab, sarilumab and anakinra in critically ill patients with COVID-19: a randomised, controlled, open-label, adaptive platform trial. Thorax. 2025 Jul 15;80(8):530-539. doi: 10.1136/thorax-2024-222488. PMID: 40360262.

Get in touch at:
AusCellDeathSociety@gmail.com