The Ex-MEN study: Exploratory genetic testing in unexplained Multiple Endocrine Neoplasia syndromes to guide clinical care and elucidate the metabolic regulation of endocrine tumours

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BACKGROUND: Multiple endocrine neoplasia (MEN) syndromes are morbid, life-limiting conditions with complex biology. The underlying cause is frequently a genetic defect altering the metabolic regulation of glandular tissue – e.g., *SDHx* variants disrupt mitochondrial function, producing pseudohypoxia and ultimately the 3P (pituitary adenoma, phaeochromocytoma, paraganglioma) association syndrome (1). *PRKAR1A* variants activate protein kinase A, resulting in excessive cAMP signalling and ultimately the widespread cell proliferation and hormone hypersecretion of Carney complex (2). Crosstalk may occur between affected tissues – e.g., in McCune-Albright syndrome, where mosaic activating *GNAS* variants lead to growth hormone excess from somatotrophinomas which directly worsens fibrous dysplasia and compressive neuropathy risk (3).

Identifying the causative variant in MEN syndromes provides a molecular diagnosis, guides tumour surveillance and treatment selection, informs reproductive planning, and facilitates cascade testing (4, 5). Tumour surveillance in *SDHB* variant carriers yields a survival benefit (6). However, many people with MEN syndromes lack an identifiable variant on standard genetic testing – representing a missed opportunity for precision care. In familial pituitary tumours, often coexisting with other tumours, approximately 80% of patients receive negative results from targeted gene panels (7).

Exploratory testing – using cutting-edge genetic technologies not yet available in standard clinical practice to examine unanalysed regions of known genes and previously unstudied genes – may reveal occult variants that can facilitate gene-specific healthcare. In my group, hypothesis-free, gene-agnostic exploratory testing has led to diagnostic success – e.g., we identified a deep intronic *SDHC* variant via exome sequencing in families with unexplained succinate dehydrogenase-deficient neoplasms (8); this variant is now routinely tested in clinical laboratories (SA Pathology, Peter MacCallum Cancer Centre etc). By contrast, targeted candidate gene approaches have not been successful (9).

In the Ex-MEN study, we will recruit patients with MEN syndromes and negative results on standard genetic testing via the SA Endocrine Genetics Clinic and the EndoGen National Endocrine Genetics MDT Meeting (both led by my group head, A/Prof Sunita De Sousa), using pre-existing consent models. We will perform exploratory genetic testing of paired germline/tumour samples using the full methodological repertoire of SA Pathology (whole exome sequencing [WES], whole genome sequencing [WGS], and RNA-Seq) to identify novel genetic causes of MEN. This builds on our prior single-gland exploratory studies that have revealed novel monogenic diabetes variants (10, 11) and new relationships between pituitary adenomas and *CHEK2* (12) and *PAM* (13). New gene-disease relationships identified in Ex-MEN will be evaluated via ancillary collaborative studies, as currently underway in other projects in my group – e.g., rat tumour cell line studies to investigate our proposed *CHEK2*/pituitary adenoma link, and CRISPR-based transactivation of patient skin cell lines to interrogate an intronic *HNF1A* variant via the University of Adelaide PERSYST study.

With my extensive track record in cancer biology, this study will be the pivotal next step in my career path as an endocrine tumour postdoctoral scientist. Ex-MEN will leverage our unique clinical/laboratory capabilities in the SA Pituitary Research Group and our vast networks to deliver a study that will directly improve genetic test delivery in Australia and elucidate molecular mechanisms underlying endocrine tumours.

AIMS: To identify novel genetic causes of MEN syndromes in patients to inform clinical care and reveal new gene-disease relationships underlying the metabolic regulation of endocrine tumours.

HYPOTHESIS: Exploratory genetic testing will reveal both occult variants in established MEN genes and variants in new candidate MEN genes that have been missed by standard genetic testing.

METHODS: This nationally recruiting translational study will be based at the SA Endocrine Genetics Clinic and the Centre for Cancer Biology. As an experienced postdoctoral scientist, I will lead the study design*, specimen retrieval, DNA extraction*, WES/WGS, RNA-Seq*, tumour immunohistochemistry*, cell line experiments* and genomic/molecular data analysis*. I will also assist in patient recruitment and phenotyping. These responsibilities are based on my PhD/early postdoctoral experience in personally conducting such work (*) and will be undertaken with my combined clinical/scientific study team. I will employ state-of-the-art multimodal methodologies to increase diagnostic yield: WES/WGS to identify sequence and copy number variants (CNVs) in known and candidate genes, including deep intronic variants; RNA-Seq to define expression patterns to confirm putative splicing/activating/inactivating variants and assess gene expression in tissues/tumours; and cell line models to evaluate new gene-disease links.

Recruitment: Participants will be recruited locally through the statewide SA Endocrine Genetics Clinic, and nationally via the EndoGen National MDT Meeting and by enlisting interstate co-investigators. This will be assisted by my supervisor, A/Prof Sunita De Sousa, who leads the SA Endocrine Genetics Clinic and EndoGen MDT and has undertaken similar exploratory testing studies in single-gland disorders. These have

involved national recruitment using a streamlined study/genetic testing consent form, phone/mail correspondence and collaboration with local clinicians. Eligible patients will be those with a personal history of MEN, or a personal history of an endocrine tumour and a family history of plausibly related endocrine tumours, and negative results on standard genetic testing. Ideally, tumour specimens will be available for paired germline/tumour testing. My laboratory is experienced in DNA studies using either historical formalin-fixed paraffin-embedded tumour specimens or fresh frozen biobanked tissues.

Sample size: As an exploratory study, sample size will be governed by access to ongoing study funding. In general, 36 patients are seen annually in the SA Endocrine Genetics Clinic and 24 patients are discussed in the EndoGen MDT Meetings, with a similar number of additional patients reviewed offline with interstate clinicians. Assuming 50% of cases relate to unexplained MEN, approximately 42 (=0.5x(36+24+24)) potentially eligible patients are expected in a 12-month period, exceeding our planned sample size of n=24. Potential participants already identified in SA include patients with: concurrent medullary thyroid cancer/primary hyperparathyroidism, pituitary adenoma/pancreatic neuroendocrine tumours, pituitary adenoma/craniopharyngioma, and multifocal paragangliomas.

WES/WGS: All coding (WES) +/- non-coding (WGS) regions will be captured and sequenced using the Illumina NextSeq platform. Variant calling and annotation will be conducted using the Genome Analysis Toolkit (GATK). Variants will be filtered based on: population frequency (e.g., gnomAD), *in silico* prediction tools (e.g., REVEL), biophysicochemical properties (e.g., AlphaFold) and family segregation data if available. CNV will be called using in-house scripts.

RNA-Seq: mRNA expression of all coding genes will be assessed using the Illumina TruSeq library construction protocol, with non-stranded, polyA+ selection, followed by automated quantitative PCR.

Tumour studies: Tissue specimens will be tested by various means – e.g., RNA-Seq, immunohistochemistry and metabolomic profiling as we/our collaborators have done previously to identify tumour markers supportive of Knudson's two-hit hypothesis for candidate tumour suppressor genes (8). Complementary germline/tumour genetic data will vastly improve the study's power to find missed genetic causes of MEN.

Cell line models: Tumour-relevant cell lines will be transfected with variants of interest. Expression in the mutated cells will be assessed by RNA-Seq/RT-PCR and functional assays, depending on anticipated variant effects. This builds on my current work in the SA Pituitary Research Group, where I have knocked out *CHEK2* in GH3 rat pituitary tumour cell lines and I am currently analysing cell proliferation, DNA damage and growth hormone/prolactin secretion.

Result disclosure: Clinically significant results will be returned to patients and their referring clinicians, with the opportunity for confirmatory NATA-accredited testing through affiliated clinical genetic services.

Timeline: I will publish the pilot data (n=24) after 12 months; the study will continue pending further funding.

OUTCOMES: A subset of patients is expected to have a newly identified genetic cause for their MEN syndrome, with the potential to transform their healthcare and that of their families. This includes providing a molecular diagnosis, guiding tumour surveillance/treatment, informing reproductive planning and enabling cascade testing. The percentage diagnostic yield of exploratory tests will inform the clinical utility of the different modalities. These findings will guide clinical service development and support ESA/EndoGen campaigns for MBS items for endocrine gene panel testing. Notably, phaeochromocytoma/paraganglioma syndrome gene panel testing (i.e., pertaining to MEN syndromes) was the only one of five endocrine gene panels proposed by ESA/EndoGen that was selected by the RCPA for a College-supported MSAC application. This is a crucial turning point in establishing it as the first MBS-funded endocrine gene panel test. Discoveries from Ex-MEN will also inform future SA Pathology gene panel design and be investigated in international cohorts via our existing collaborations – e.g., the NIH and Institut Cochin (pituitary adenoma collaborators) and Exeter Laboratory (MODY collaborators). Scientifically, identifying novel variants/genes in model MEN cases will provide insights into the mechanisms of endocrine tumorigenesis and shed light on the regulation of cell cycle and hormone biosynthesis pathways in the neoplastic transformation of endocrine tissues. New gene-disease relationships and the utility of exploratory testing may be incorporated in future guidelines, noting our group's track record in endocrine tumour guideline development (14-16).

BUDGET: $110,480 of consumable funds are available through an existing RAH Project Grant (ref.126-02-01-09-25), expected to cover 24 participants at ~$4,600 of exploratory genetic testing per family (selected tests will differ between cases). However, stipend support is not available. **The ESA Ken Wynne Award would provide vital salary support, enabling me to undertake this study. Without securing additional funding, the Ex-MEN study – and my ongoing career development in the endocrine tumour field – will not be possible as my current contract ends in June 2026 with no other available salary support.**

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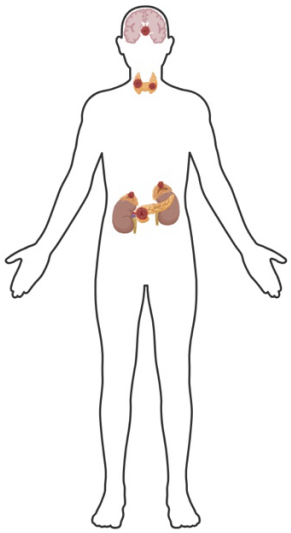


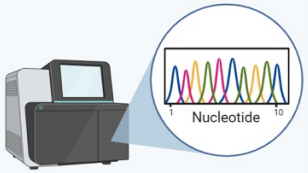
Outcomes

- Molecular diagnosis
- Guided tumour surveillance & treatment
- Informed reproductive planning
- Enabled cascade testing

Recruitment

- **SA**: SA Endocrine Genetics Clinic
- **Nationally:** EndoGen National MDT Meeting & via co-investigators

WES/WGS



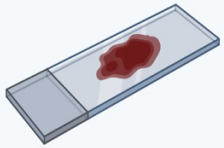
- Candidate gene-targeted analysis
- Variant-targeted analysis

RNA-Seq

- Analysis of mRNA expression of all coding genes
- Confirmatory qPCR

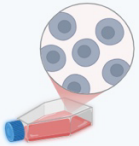
Tumour studies

- WES, WGS, RNA-Seq
- Immunohistochemistry
- Metabolomic profiling



Cell line models

- Use of tumour-relevant cell lines
- Functional assays
- Analysis of cell proliferation & hormone secretion



Result disclosure

- Clinically significant results will be returned to patients/referring clinicians
- Confirmatory NATA-accredited testing

ABRIDGED CV: Dr Alexandra Sorvina (Alexandra.Sorvina@sa.gov.au)
SA Pituitary Research Group, Centre for Cancer Biology, SA Pathology/University of South Australia

I am a grant-funded scientist at the Centre for Cancer Biology, an alliance between University of South Australia and SA Pathology. I moved into the rapidly growing South Australian Pituitary Research Group in August 2025 after successfully securing a 12-month contract and I intend to continue my career path in translational endocrine tumour research if further salary support can be attained.

I have an undergraduate degree in genetics and a PhD in cell biology (completed in 2015), with extensive training in cell biology, cancer biology, histopathology and imaging – all of which are directly relevant to the Ex-MEN study.

I have a strong ability to execute research projects, with a particular capability to integrate knowledge across multiple disciplines and produce high-quality research outputs. I have authored 37 publications, including ten as first author and one as senior author, in journals such as *Pathology*, *Scientific Reports* and *Oncotarget*.

During my postdoctoral years, I have contributed directly and intellectually to biomarker development programs across a range of cancers (e.g., prostate, ovarian, pancreatic, colorectal, skin and breast). I have been responsible for study and experimental design, implementation, data analysis and presentation, and problem solving. From this work, methods for confirming detection and evaluating the progression of prostate cancer have been developed, for which I am a co-inventor (patent: AU2020343723A1).

I have served as a Chief Investigator (CI) and contributed to multiple successful grant applications, collectively worth approximately $17 million during my postdoctoral career. In addition, I have played a strong role in student training and engagement, particularly in cancer cell biology. I have co-supervised two PhD students to completion, and I am currently co-supervising another PhD student at University of South Australia.

Having joined the SA Pituitary Research Group, my postdoctoral work is currently focused on analysing *CHEK2* and *ESR1* variants in a rat pituitary tumour cell line model (GH3). With my strong track record in translational research and expertise in cancer cell biology, I am well-positioned to address a critical knowledge gap in MEN syndromes in patients with negative results on standard genetic testing.

QUALIFICATIONS:

2011 – 2015 Doctor of Philosophy, University of South Australia, Adelaide, Australia

2005 – 2010 Specialist Diploma in Genetics (Equivalent to a Master's degree in Europe), Kazan (Volga region) Federal University, Kazan, Russian Federation

APPOINTMENTS:

Nov 2022 – Current Grant-Funded Scientist (serial contracts), SA Pathology, Adelaide, Australia

Jan 2020 – Oct 2022 Research Fellow, University of South Australia, Adelaide, Australia

Apr 2015 – Dec 2019 Research Associate, University of South Australia, Adelaide, Australia

Jan 2015 – March 2015 Research Assistant, University of South Australia, Adelaide, Australia

PUBLICATION HISTORY:

I have authored 37 peer-reviewed publications, including ten first-author and one senior-author papers (H-index 12), and have contributed to three provisional patent applications.

Journal articles

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29. Chernov, V, Chernova, O, Medvedeva, E, **Sorvina, A**, Davydova, M, Rogova, M & Serebryakova, M 2010, 'Responses of *Acholeplasma laidlawii* PG8 cells to cold shock and oxidative stress: Proteomic analysis and stress-reactive mycoplasma proteins', Doklady Biochemistry and Biophysics, vol. 432, no. 1, pp. 126-130.

Reviews
30. Lam, GT, Prabhakaran, S, **Sorvina, A**, Martini, C, Ung, BS, Karageorgos, L, Hickey, SM, Lazniewska, J, Johnson, IR, Williams, DB, Klebe, S, Malone, V, O'Leary, JJ, Jackett, L, Brooks, DA & Logan, JM 2022, 'Pitfalls in cutaneous melanoma diagnosis and the need for new reliable markers', Molecular Diagnosis and Therapy, vol. 27, no. 1, pp. 49-60.
31. ***Sorvina, A**, *Antoniou, M, Esmaeili, Z & Kochetkova, M 2023, 'Unusual suspects: bone and cartilage ECM proteins as carcinoma facilitators', Cancers, vol. 15, no. 3, article no. 791, pp. 1-24.
***First equal authors**
32. Hickey, SM, Ung, B, Bader, C, Brooks, R, Lazniewska, J, Johnson, IR, **Sorvina, A**, Logan, J, Martini, C, Moore, CR, Karageorgos, L, Sweetman, MJ & Brooks, DA 2022, 'Fluorescence microscopy-an outline of hardware, biological handling, and fluorophore considerations', Cells, vol. 11, no. 35, pp. 1-32.
33. Stevens, K, Bader, C, **Sorvina, A**, Plush, S & Morrison, J 2017, 'Imaging and lipidomics methods for lipid analysis in metabolic and cardiovascular disease', Journal of Developmental Origins of Health and Disease, vol. 8, no. 5, pp. 566-574.

Book Chapter
34. Shandala, T, R Kakavanos-Plew, Ng, Y, Bader, CA, **Sorvina, A**, Parkinson-Lawrence, E, Brooks, RD, Borlace, G, Prodoehl, M & Brooks, D 2012, 'Molecular machinery regulating exocytosis', in R Weigert (ed.), Crosstalk and integration of membrane trafficking pathways, InTech, Croatia, Ch. 4, pp. 61-108.

Conference papers or abstracts
35. Zhang, WQ, Morrison, JL, Darby, JR, Plush, S, **Sorvina, A**, Brooks, D, Monro, TM & Afshar Vahid, S 2017, 'A fibre optic fluorescence sensor to measure redox level in tissues', Nanophotonics Australasia 2017, SPIE, vol. 10456, article no. 104564R, pp. 1-6.

Other publications
36. Bader, C, **Sorvina, A**, Darby, J, Lock, M, Soo, JY, Johnson, I, Caporale, C, Massi, M, Stagni, S, Morrison, J, Plush, S & Brooks D 2018, 'Imaging mitochondria in live or fixed muscle tissues', Protocol Exchange*, doi:10.1038/protex.2018.101.
An open repository of community-contributed protocols sponsored by the journal Nature Protocols
37. Ung, B, Logan, J, **Sorvina, A**, Martino, C, Prabhakaran, S, Karageorgos, L & Brooks, D 2019, Prostate cancer biomarker atlas.

Manuscripts pending
1. Mignone, E, **Sorvina, A**, Torpy, DJ, Scott, HS & De Sousa, SMC, The genetic landscape of pituitary tumours: an examination of pituitary adenomas, craniopharyngiomas, pituitary blastoma, pituicytomas and hypothalamic tumours', submitted to *Journal of Clinical Endocrinology & Metabolism*.
2. Ovenden, CD, Candy, N, Bacchi, S, **Sorvina, A**, Castle-Kirszbaum, M, Poonnoose, S, Vrodos, N, Jukes, A, Santoreneos, S, Torpy, DJ, Psaltis, A & De Sousa, S, 'Systematic Review of the Molecular Basis for Cavernous Sinus Invasion in Somatotropinomas', submitted to *Endocrine-Related Cancer*.

3. Maggacis, R**, Sorvina, A**, Hayes, LJ, Inder, WJ, Brooks, EK & De Sousa, SMC, 'A Contemporary Review of Multiple Endocrine Neoplasia Syndromes', at final stages of preparation for *Endocrine Oncology*.
4. Lam, GT, Martini, C, **Sorvina, A**, Hickey, SM, Hindes, MT, Waugh, D, O'Leary, JJ, Brooks, DA & Logan, JM, 'Implications of altered endosomal-lysosomal biogenesis in melanoma pathogenesis', submitted to *International Journal of Molecular Sciences*.

AWARDS:

2025 Publication Accelerator Award (~7k), University of South Australia

2020 Academic Promotion to Level B, University of South Australia

2019 Research Award Finalist; University of South Australia, Research Excellence Category, Early Career Researcher

PATENTS:

1. Brooks, DA… **Sorvina A** et al, AU2020903662, Methods for Confirming Detection and Evaluating the Progression of Colorectal Cancer, EnVision Sciences (Provisional patent, Australia).
2. Brooks, DA… **Sorvina A** et al, AU2020903665, Methods for confirming detection and evaluating the progression of ovarian cancer, EnVision Sciences (Provisional patent, Australia).
3. Brooks, DA… **Sorvina A** et al, PCT/AU2020/050925, Methods for confirming detection and evaluating the progression of a prostate cancer, EnVision Sciences (Provisional patent, Australia).

GRANTS:

Since 2016, I have co-led the development of diagnostic and prognostic markers across a range of cancers and have served as CI on multiple grants. The grants listed below cover the five-year period from 2020, adjusted for career disruption. In total, I have been the Principal or Co-investigator in successful grants amounting to approximately $17 million during my postdoctoral career.

2024 Kochetkova, M, **Sorvina, A**, Farshid, G, Bochner, M & Szpak, Z, ' Charting the tumour stroma landscape to find better ways for the treatment of breast cancer', Cancer Council SA, $85,000.

2022 Brooks, DA, O'Leary, JJ, Brooks, RD, Logan, J, **Sorvina, A**, Martino, C, Butler, L, Johnson, I, Hickey, S, Selemidis, S, Parkinson-Lawrence, EJ, Orgeig, S, Lazniewska, J, Thomas, C, Ung, B, Bader, C, Chappell, N, Moore, C, Reynolds, P, Esterman, A & Karageorgos, L, ' Diagnosis and prognosis of cancer using blood and tissue tests', Envision Sciences Pty. Ltd., $3,900,000.

2020-2022 Brooks, DA, O'Leary, JJ, Pursey, P, Morretti, K, Klebe, S, Samaratunga, H, Delahunt, B, Karageorgos, L, Esterman, A, Dinan, A, Brooks, RD, Logan, J, **Sorvina, A**, Martino, C, Butler, L & Ung, B, 'Diagnosis and prognosis of prostate cancer using blood and tissue tests', Envision Sciences Pty. Ltd./UniSA BTB Grant (MTP connect MRFF), $2,400,000.

2019-2022 Brooks, DA, Logan, J, Martino, C, **Sorvina, A**, Johnson, I, Butler, L, Selemidis, S, O'Leary, J & Pursey, P, ' UniSA Support Grant for Cancer Research Translation Programme', UniSA Division of Health Sciences ($125,000/yr) and UniSA Innovation Services ($283,000/yr), $1,632,000 ($408,000/yr).

2020-2021 Brooks, DA, Logan, J, Martino, C, **Sorvina, A**, O'Leary, J & Karageorgos, L, 'Endosomal biomarkers to define melanoma pathogenesis', Rattigan Family Trust, $33,330/ year.

2020 Brooks, DA, O'Leary, JJ, Brooks, RD, Logan, J, **Sorvina, A**, Martino, C, Butler, L, Johnson, I, Hickey, S, Selemidis, S, Parkinson-Lawrence, EJ, Orgeig, S, Lazniewska, J, Thomas, C, Dale, B, Ung, B, Bader, C, Morrow, I, Chappell, N, Moore, C, Reynolds, P, Esterman, A & Karageorgos, L, ' Development Program: Biomarkers and therapeutics for prostate and other cancers', Envision Sciences Pty. Ltd. Translational Research Grant, $2,000,000.

CONTRIBUTIONS TO FIELD:

Since 2020, I have served as a Guest Editor for the journal *Cells*, overseeing the Special Issue 'Where Chemistry and Biology Meet to Develop New Cellular Imaging Technologies', which published five papers. I am also an invited reviewer for the for the journal *Pathology*.

Following my transition to the SA Pituitary Research Group this year, I soon after became a full basic science member of ESA. If successful in continuing my career path as an endocrine tumour postdoctoral scientist, I hope to meaningfully bring my basic science experience to ESA, particularly by joining the ESA Mentorship Program to be a mentor to junior basic science researchers and/or emerging clinician-scientists, and contributing if possible, to the ESA Scientific Strengthening Committee to advocate for the growth of translational and discovery endocrine science in Australia.

CAREER DISRUPTION STATEMENT

There have been several disruptions to my career that affected my research output. Firstly, the need to protect commercially sensitive data and significant intellectual property (IP) restricted the publication of research findings until commercialisation millstones were achieved. This limited my publication rate up to 2022.

In addition to these constraints, the COVID-19 pandemic (2020-2021) significantly impacted access to human tissues, laboratory facilities and clinical trials. Nevertheless, my research trajectory remained strong, with five papers published during this period.

I took a 11-month career break for parental leave (May 2021 – April 2022), during which I was on continuous leave with no access to laboratory facilities. This led to delays in completing studies, data collection and analysis, and manuscript preparation/submission. Despite this extended period of absence and ongoing caring responsibilities, I have published five papers during the current capture period and applied for three competitive funding opportunities (e.g., NHMRC Investigator Grant, CSL Fellowship and Florey Fellowship).

Upon returning to work, my FTE was reduced from 1.0 to 0.6 from April to October 2022 due to childcare responsibilities, followed by a five-week period of leave in October 2022. More recently, in August 2025, my FTE was again reduced from 1.0 to 0.8. Despite these career interruptions and reduced working hours, my research track record remains on an upward trajectory – with 37 published papers to date, four manuscripts under review, and contributions to three provisional patents.

University of South Australia

Name	Alexandra Sorvina
Student ID	110072508
Issue Date	31 August 2015

Official Academic Transcript

Program Summary

Current Programs

Program Code	IPHD
Program Name	**Doctor of Philosophy**
Status	Completed Program

Year	Program	Course Code	Course Description	Units	Grade
2014	IPHD	PHAR 8010	FT Research (Pharmacy)	18.00	Non Graded Pass
	IPHD	PHAR 8010	FT Research (Pharmacy)	18.00	Ongoing Assessment
2013	IPHD	PHAR 8010	FT Research (Pharmacy)	18.00	Ongoing Assessment
	IPHD	PHAR 8010	FT Research (Pharmacy)	18.00	Ongoing Assessment
2012	IPHD	PHAR 8010	FT Research (Pharmacy)	18.00	Ongoing Assessment
	IPHD	PHAR 8010	FT Research (Pharmacy)	18.00	Ongoing Assessment
2011	IPHD	PHAR 8011	FT (SP5) Research (Pharmacy)	18.00	Ongoing Assessment

End of Academic Record

Allan Tabor
Academic Registrar

Page 1 of 2

University of South Australia

Name	Alexandra Sorvina
Student ID	110072508
Issue Date	31 August 2015

UNIVERSITY OF SOUTH AUSTRALIA ASSESSMENT NOTATIONS

The University of South Australia was formed on 1st January 1991 by the amalgamation of the South Australian Institute of Technology and the Magill, Salisbury and Underdale campuses of the South Australian College of Advanced Education.
A full listing of antecedent institutions is available at www.unisa.edu.au

UNIVERSITY OF SOUTH AUSTRALIA

Coursework Notations

HD	High Distinction	85-100%
D	Distinction	75-84%
C	Credit	65-74%
P1	Pass Level 1	55-64%
P2	Pass Level 2	50-54%
F1	Fail Level 1	40-49%
F2	Fail Level 2	Below 40%
NGP	Non-graded Pass	50-100% (course assessed on a pass/fail basis only)
F	Fail	0-49% (course assessed on a pass/fail basis only)
SP	Supplementary Pass	50% (introduced in 1996 for a course passed on the basis of a supplementary assessment)
CP	Conceded Pass	Notional percentage not applicable
TP	Terminating Pass	Notional percentage not applicable
W	Withdrawn	Withdrew without penalty
WF	Withdrawn Fail	Withdrew after the date prescribed for withdrawing without penalty
****	No Grade Recorded	No grade recorded at the time of printing
I	Incomplete	Extension of time granted to complete the assessment
AS	Advanced Standing	Advanced Standing for prior studies
T	Credit Transferred	Credit transferred from another institution
AUD	Audit Student	Enrolment on a single-course basis with no assessment completed

Honours Notations (for Honours degrees and degrees with honours)

Honours First Class	Outstanding example of scholarship
Honours Second Class A	High level of scholarship and performance in both the coursework and research components
Honours Second Class B	Substantial performance in application and scholarship across the program
Honours Third Class	Performance at a satisfactory level and completion of the requirements
F	Unsatisfactory performance in the program

Research Notations (for Doctor of Philosophy, Masters by research and Professional Doctorates by research)

O	Ongoing	Assessment continues in a subsequent study period
NGP	Non-graded Pass	Met specified assessment criteria to required standard
SE	Suspended - Examined	Thesis examined, revisions required, candidate elects not to complete. Reinstatement may be permitted
SNE	Suspended - Not Examined	Requirements not met, candidate suspended prior to examination. Reinstatement may be permitted
T	Terminated	Unsatisfactory progress against established milestones. Reinstatement not permitted
F	Fail	Thesis failed examination. Reinstatement not permitted

The explanation of grades was current at 1 August 2005. Subsequent amendments and a full explanation of any assessment notations will be published in the relevant academic policies at www.unisa.edu.au

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KOLLING
Institute of
Medical Research

IN CONFIDENCE

Endocrine Society of Australia
31st October 2025

To Whom It May Concern,

Re: Dr Alexandra Sorvina

I am writing as an external reviewer to support Dr Alexandra Sorvina and their application for the Endocrine Society of Australia Ken Wynne award. I have read her project in detail, entitled "The Ex-MEN study: Exploratory genetic testing in unexplained Multiple Endocrine Neoplasia syndromes to guide clinical care and elucidate the metabolic regulation of endocrine tumours."

Regarding the proposal, this brings state-of-art genetic sequencing technology to identify novel genetic drivers in hereditary endocrine neoplasia syndromes. Historically, these syndromes have been a rich source of discovery and yet our understanding of the genetic architecture of these diseases remains incomplete. *A priori*, the proposed study is likely to yield novel and meaningful genetic discoveries. Analyses will include whole exome and whole genome sequencing, RNA-seq, tumour studies and validation in cell line models. The proposal is scientifically sound and technically feasible. The findings are likely to be reported at major scientific meetings and published in leading specialty journals.

With respect to the applicant, Dr Alexandra Sorvina is a rising star: a basic scientist with a primary background in cancer biology who is now transitioning into endocrine cancers, and her skills are sorely needed in this area. Her track record is impressive relative to opportunity. She has 37 peer-reviewed publications including 10 first author publication in 1 senior author publication. She has a number of patents. She has had strong success in grant funding. She has contributed her expertise as editor and reviewer for relevant scientific journals. I note the career disruption statement which has been moderately impactful to career progression.

With respect to the facilities available for the study, this will be conducted at the Centre for Cancer Biology within the SA pituitary research group. The facilities and scientific support are exemplary for this type of research, supported by mentorship of A/Professor De Sousa and Professor Scott. This group has already made seminal contributions to the field of endocrine cancer genetics and genomics.

I offer my wholehearted support for this application. It has a high likelihood of success and impactful discovery. Dr Sorvina would be a worthy recipient of the Ken Wynne award and I have no doubt will make a strong contribution to the Endocrine Society of Australia in the future.

Yours Sincerely,

Professor Roderick Clifton-Bligh
Head, Cancer Genetics Laboratory
Kolling Institute
Royal North Shore Hospital and University of Sydney

Telephone: +612 9463 1680 Fax: +612 9463 1045 email: roderick.cliftonbligh@sydney.edu.au

15th October 2025

To the ESA Selection Panel:

Re: ESA Ken Wynne Memorial Postdoctoral Research Award application, Letter from the Head of the Department for Dr Alexandra Sorvina

I write as the Head of Department and line manager for Dr Sorvina. This is to certify that Dr Sorvina's project entitled 'The Ex-MEN Study: Exploratory genetic testing in unexplained Multiple Endocrine Neoplasia syndromes to guide clinical care and elucidate the metabolic regulation of endocrine tumours' will be conducted in the Centre for Cancer Biology within the SA Pituitary Research Group. I confirm that appropriate facilities and scientific support are available for this ambitious research project which is set to expand genetic testing options for people in Australia with unexplained endocrine tumours, whilst also offering potentially transformative biological insights in how endocrine tumours develop.

Dr Sorvina has consistently demonstrated excellence in her research and is well-positioned to make significant contributions to this program. With 37 peer-reviewed publications and direct involvement in multiple cancer-related patents, she has established a strong track record of delivering impactful research outcomes. Dr Sorvina has played an integral role in the biomarker discovery program during her postdoctoral years. In recognition of her achievements, she was a finalist for the UniSA Early Career Researcher Award – further underscoring her potential and promise in Australian medical research. Dr Sorvina brings the knowledge, technical expertise, and leadership necessary to ensure the success of the proposed research project, and I have full confidence in her ability to deliver high-quality results.

Noting that this application is to the Endocrine Society of Australia, it is important to recognise that Dr Sorvina is an accomplished cancer biology scientist who has recently actively transitioned from research in common solid organ malignancies (breast, prostate, colorectal) to focus on endocrine tumours – this is an unequivocal win for endocrine neoplasia research in Australia if this career path can be sustained. Her move has been facilitated through a short-term contract – that is regrettably unable to be extended beyond July 2026 – and inclusion of Dr Sorvina in the pioneering new South Australian Pituitary Research Group founded in 2024 by my former PhD student, A/Prof Sunita De Sousa, who is herself an internationally regarded expert in endocrine tumour genetics as evidenced by her 60+ publications, key discoveries of new endocrine genetic causes, selection in international guidelines groups and invitations to speak in the last 12 months by the peak endocrine societies of Asia, Europe and the US.

Dr Sorvina is the sole basic scientist employed in A/Prof De Sousa's research group and is crucial to the group's aims to undertake true discovery science that sheds light on how endocrine tumours develop and may be targeted. Dr Sorvina and A/Prof De Sousa are currently co-leading cell line studies of proposed pituitary tumorigenesis genes, with these publications anticipated around the end of Dr Sorvina's contract. Provided further funding can be secured at that time, I have no doubt that the partnership of these two formidable young women in science/medicine, both of whom have successfully navigated recent maternity leave career interruptions, will transform our understanding of endocrine tumours. I believe this is precisely the sort of early career scientific/clinical collaboration that the Endocrine Society of Australia should support to ensure Australia's success in endocrine science in the next generation, remembering that young groups such as this lack the financial buttresses of long-established research groups.

Yours Sincerely,

Professor Hamish Scott
Head of Department, Genetics and Molecular Pathology | SA Pathology
Centre for Cancer Biology, An SA Pathology & UniSA alliance
Phone:| 08 8222 3651 | Email: Hamish.Scott@sa.gov.au
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