University of Southampton

THE ODDFELLOWS SOCIETY PHD STUDENT FINAL UPDATE:

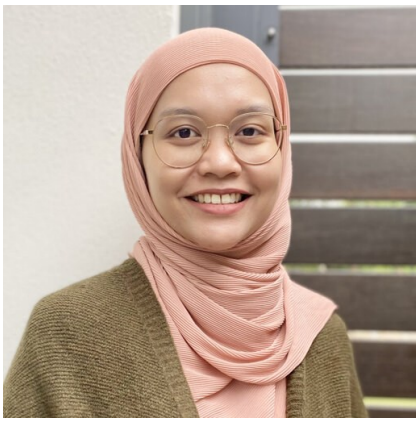
Nur Zainal

2025

SOUTHAMPTON TOGETHER

THE IMPACT OF YOUR SUPPORT

Thanks to the inspiring generosity of The Oddfellows Society, our researchers have continued their incredible work in the Centre for Cancer Immunology. For the past three years, your support has funded Nur Zainal's PhD scholarship. We are delighted to share with you her final report along with an update from her supervisor, Professor Tim Fenton.



I would like to express my sincere gratitude for your generous support over the past three years. Your funding has played a pivotal role in enabling me to pursue my PhD and carry out research that I am genuinely passionate about. This support has not only impacted my personal growth as a scientist but has also significantly advanced our research into developing a better model for studying lung cancer.

Thanks to your contribution, we were able to initiate a pilot characterisation of a novel humanised mouse tumour model. Findings from this study demonstrate that our model holds significant promise in transforming preclinical cancer research. Notably, our humanised model more accurately reflects the complexity and behaviour of human cancers- particularly in terms of genetic diversity, immune interaction, and drug resistance. This advancement has the potential to improve the reliability of preclinical testing, accelerate the development of more effective cancer therapies and vaccines, and ultimately bring us closer to treatment strategies that work better for patients.

Key Findings & Impact

We began by addressing a fundamental limitation in current lung cancer mouse models: the absence of human APOBEC3 genes, which are a known source of mutations that contribute to drug resistance in lung cancer patients. By introducing the full set of human APOBEC3 genes into our model, we were able to observe tumour behaviour that much more closely mirrors human lung cancer.

Highlights from our study include:

- Human-like APOBEC3 gene expression: The seven APOBEC3 genes in our model showed an expression pattern highly correlated with those found in human lung cancers, reinforcing the model's physiological relevance.
- Enhanced immune cell activity: We observed a significant increase in immune cell infiltration, particularly activated macrophages and deeply infiltrated T-cells, suggesting that the humanised tumours are producing more neoantigens (new abnormal proteins made by cancer cells), making them more detectable to the immune system.
- Development of cell lines: We have successfully established multiple lung cancer cell lines from the humanised tumours, allowing us to conduct more experiments with fewer animals – important from both an ethical and cost perspective.
- Drug resistance modelling: Preliminary results show that APOBEC3 activity in our model increases in response to drug treatment, similar to what is seen in cells derived from human lung cancer patients. This validates the use of our model to study mechanisms of drug resistance and identify novel therapeutic targets.

These results enabled us to secure additional funding to support more detailed investigations. We are now preparing additional grant applications to further develop and expand the utility of this model.

Next Steps

My current work focuses on identifying the most robust APOBEC3-driven mutations and the unique mutant proteins they produce, especially those that enable tumour cells to survive treatment. These could serve as the basis for new cancer vaccine strategies aimed at eliminating drug-resistant tumours.

We are also applying our novel humanised-APOBEC3 mouse model to study resistance mechanisms to an exciting new class of cancer drug called RAS inhibitors (RASi) in lung cancer. This is particularly timely, as at least 40 RAS inhibitors are currently undergoing clinical trials, and the hold enormous potential for the effective treatment of some of the most deadly human cancers (including lung, pancreas and colorectal cancer), yet drug resistance (likely driven at least in part by APOBEC) remains a major barrier to their long-term effectiveness. We hope this research will contribute to more effective, personalised treatment strategies for RAS-driven cancers.

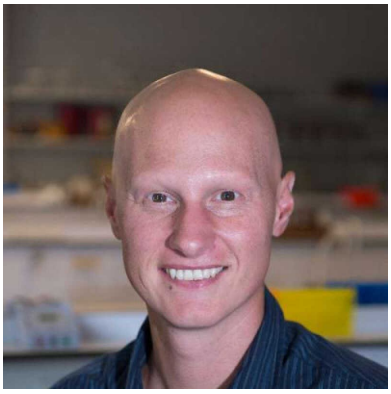
Looking Ahead

The support from the Oddfellows has allowed me to grow immensely both professionally and personally. Over the past three years, I have gained invaluable technical and analytical skills, deepened my expertise in *in vivo* modelling, and developed a strong foundation for a future research career focused on translational cancer biology.

Looking forward, I am excited to continue refining this model and exploring its relevance across other cancer types. I aim to establish a long-term research niche in humanised cancer modelling and drug resistance- ultimately working towards preclinical tools that better serve patients. Once again, thank you for making this research possible. Your contribution is making a tangible difference, and I am incredibly grateful.

With warm wishes,
Nur Zainal

A NOTE FROM TIM FENTON



I would also like to express my sincere gratitude to the Oddfellows Society for their generous support of Nur's PhD project. Nur is an exceptional PhD student; she has developed what I am sure will be a 'go-to' model of lung cancer for researchers aiming to develop new treatments for this deadly disease.

Nur's work underpins a £1.2M grant I have recently submitted to the Medical Research Council to continue to develop this project, with the intention that Nur remains with us as a Postdoctoral Researcher for at least the next three years. I am also pursuing exciting collaborations with industry partners (Genentech (USA) and AstraZeneca (UK)), to help ensure Nur's findings are translated into therapeutic strategies that will provide patient benefit as fast and effectively as possible. None of this would have been possible without the support of the H. A. Andrews Memorial Fund. It was a pleasure to attend your annual conference with Nur in May to give a brief summary of her work and I will be very happy to keep you updated as this project progresses, should that be of interest to the Society.

Best wishes,
Professor Tim Fenton

Thank you for your generous support which is funding life-saving cancer treatments. Your gift enabled investment in ground-breaking research and the development of brilliant new researchers. Once again, thank you.

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