How would you explain the main findings of your paper in lay terms?
The outermost layer of skin is comprised of cells called keratinocytes which divide, progressively mature, and ultimately die as they migrate towards the surface of the body. This process allows skin to constantly self-renew and form an effective barrier against external stressors. Whether keratinocytes divide or commit to maturation is controlled by epigenetic processes in which DNA and associated proteins (histones) are chemically modified. Our publication describes how two structurally similar epigenetic modifiers, KAT2A and KAT2B, have distinct and opposing functions in balancing keratinocyte self-renewal and maturation. We explored how KAT2A and KAT2B might produce differing effects and identified a histone modification that is specifically maintained by KAT2A but not KAT2B in keratinocytes. These findings not only aid our understanding of how healthy skin regenerates but also supports a role for histone modification dynamics during wound healing.

Were there any specific challenges associated with this project? If so, how did you overcome them?
We set out to comparatively assess the functions of two highly similar paralogous genes: KAT2A and KAT2B. This meant that our experiments were prone to misinterpretation if our reagents inappropriately targeted the wrong paralog. Therefore, we made efforts to assess cross-reactivity, which was made possible by our generation of single- and double-knockdown cell lines. We were also similarly cautious about the specificity of histone antibodies used, as we previously found that some commercial antibodies had high affinity towards similar or in some cases completely different histone modifications. Using histone peptide arrays proved valuable in screening out these problematic antibodies.

When doing the research, did you have a particular result or 'eureka' moment that has stuck with you?
One of the most satisfying moments during this project was when we were able to reverse our knockdown phenotype and identify the specific KAT2A domains that were functionally significant in keratinocytes. Now I am always thinking about ways to rescue cellular phenotypes.

Why did you choose Journal of Cell Science for your paper?
Throughout my career I have found Journal of Cell science to be a valuable source of high-quality epigenetics research with important links to cell biology. It’s always satisfying to read how these small chemical modifications can have such big impacts on cell function and behavior.

Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?
When I started my PhD, most core molecular biology techniques were completely new to me. Thankfully my project supervisor, Dr Chin Yan Lim, was often present in the lab and gave me a crash course in everything that I needed to know. I think supervisors that maintain connection with the practical aspects of the lab are uncommon but are certainly valuable for the development of scientists early in their career.

What motivated you to pursue a career in science, and what have been the most interesting moments on the path that led you to where you are now?
At the heart of it, I pursued a scientific career because I was fascinated by the elegant mechanisms employed by cells, and I wanted to play a part in uncovering these myself. Later down the
line I realized that academic research can also offer a great amount of freedom in how I approached my work. Being in control of my own projects in such an independent manner has always been very fulfilling. I have also taken advantage of the international nature of academic research. My career in science has allowed me to work in labs across the world, including in Singapore, which has made stepping out of the lab always exciting and interesting!

Who are your role models in science? Why?
I don’t have specific role models. Rather, there are countless times when I have been inspired by interns, students and mentors that have worked hard and had positive constructive attitudes, especially when experimental work is at its most challenging and frustrating.

What’s next for you?
I am currently a postdoc at Yale University in the midst of an exciting epigenetics project looking into cancer risk inheritance via the paternal germline. Once I’ve figured that out, I envision an academic life wrapped around even more histones.

Tell us something interesting about yourself that wouldn’t be on your CV
I am obsessed with film history, something that I share with my partner who researches technical innovation in the early days of cinema. Usually this involves me reading another Orson Welles biography, watching films about film, or visiting shooting locations whenever I travel. I also enjoy hand drawing graphical models when I get a chance (like in this paper!).

Reference
Walters, B. W., Tan, T. J., Tan, C. T., Dube, C. T., Lee, K. T., Koh, J., Ong, Y. H. B., Tan, V. X. H., Jahan, F. R. S., Lim, X.N., Wan, Y. and Lim, C. Y. (2023). Divergent functions of histone acetyltransferases KAT2A and KAT2B in keratinocyte self-renewal and differentiation. J. Cell Sci. 136, jcs260723. doi:10.1242/jcs.260723