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SCIENTIST SPOTLIGHT

Scientist Spotlight: Karen Wing Yee Yeun

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Scientist Spotlights are short articles, published periodically, that highlight established and emerging leaders in chromosome and genome research. In each article, the featured scientist answers a defined set of questions that reveal their academic and scientific path to their current position, the events or experiences that cultivated their interest in science, their own scientific discoveries that most excite them, and extracurricular activities that have shaped who they are as a scientist and human being. The Editor-in-Chief, Executive Editor, and Associate Editors of Chromosome Research will solicit scientists to be highlighted, but suggestions and/or self-nominations from the readership are also encouraged.

Editor's Note: In this series established in 2021, we ask emerging and established leaders in chromosome and genome biology to share their thoughts on science, mentoring, and career choices. The articles offer a glimpse into the diversity of research, professional paths, and perspectives on science and life within our chromosome research community.

This Scientist Spotlight focuses on **Karen Wing Yee Yuen, PhD**. Dr. Yuen was born and raised in Hong Kong. She moved to Vancouver, Canada to finish her last year of high school and did her undergraduate studies at Simon Fraser University, Canada, specializing in Molecular Biology and Biochemistry. She pursued a PhD at the University of British Columbia (Canada) in Medical Genetics in Professor Phil Hieter's lab where she studied chromosome instability (CIN) mutants in the yeast *Saccharomyces cerevisiae*. She did her postdoctoral training as a Hong Kong Croucher fellow in Dr. Arshad Desai's lab at Ludwig Institute for Cancer Research/University of California, San Diego. Her postdoctoral research focused on holocentromere identity in *Caenorhabditis elegans*. Thereafter, she returned to Hong Kong to establish her independent research lab at the University of Hong Kong where she is now an Associate Professor in the School of Biological Sciences.

Dr. Karen Wing Hee Yuen is a chromosome researcher at University of Hong Kong. Her lab uses the nematode *C. elegans* to study centromere identity and chromosome segregation.

Responsible Editors: Beth Sullivan and Rachel O'Neill

Q: How did you become interested in science and what was your path through undergraduate, graduate school, and postdoc? Were there major lessons you learned along the way?

KY: I became interested in science probably starting in secondary school, when we had a chance to perform hands-on experiments. My Physics teacher in my secondary school in Hong Kong and my Chemistry teacher in my secondary school in Vancouver, Canada would make us do the experiments ourselves instead of just believing in what they said. This seeded my curiosity in science and kind of encouraged me to design experiments to test out different things.

In secondary school, I was fascinated by deducing the inheritance of specific traits in different organisms and the calculation of probability. My interest in Genetics and Cell Biology grew while I did my Final Year Project with Dr. Lynne Quarmby in Simon Fraser University, where I worked with another single-celled green algae *Chlamydomonas* to study its flagella function and how it swims. For my PhD study, I was determined to study chromosome structure and stability, as chromosomes are the vehicles of all genes and genetic materials. Therefore, I rotated in Dr. Carolyn Brown's lab studying X-chromosome inactivation and in Phil Hieter's lab studying chromosome instability. I was attracted to using a simple, single-celled eukaryotic model organism, the budding/baking/brewing yeast, for tractable genetics, real-time imaging, and cell cycle studies. I used yeast as a model to perform a genome-wide screening of chromosome instability (CIN) mutants via a visual color assay. We discovered ~300 mutants that exhibit CIN phenotypes in yeast. Based on these candidate genes and their conserved homologs in humans, we asked whether these sets of genes were highly mutated in human solid cancers. We sampled colorectal cancer patient samples and identified that a few genes involved in sister chromatid cohesion (a cellular process required to hold the replicated sister chromosomes together after DNA replication and before they separate) are highly mutated and can contribute to CIN in human cells.

After receiving my PhD, I went to Arshad Desai lab at Ludwig Institute for Cancer Research/University of California, San Diego, as a Hong Kong Croucher post-doctoral fellow to study holocentromere identity in *C. elegans* and the segregating behavior of extra-chromosomal arrays or artificial chromosomes formed from injected DNA. The use of different model organisms prompted me to think and choose the most suitable model to answer the existing question. Along the way, I learned to identify important yet unanswered scientific questions, and at the same time to evaluate one's strength and weakness and find your own niches to help to tackle the problems. You have to enjoy what you are doing to push you through.

Q: What is the most exciting discovery you have made in your own research program and/or could you describe a recent line of work of which you are most proud?

KY: The most exciting discovery I have made in my own research program is to provide insights to the epigenetic regulation of centromere function. The centromere has been traditionally viewed as a compact, inert region on the chromosome that is devoid of genes and transcription activity. However, in the last decade, it has been shown that transcription through the centromere in many species is indeed important for its function. Our lab showed that even short, point centromeres from simple, single-celled eukaryotic organism *Saccharomyces cerevisiae*, that is the baking or brewing yeast, require transcription to maintain centromere function.

A recent line of work that I am most proud of is on the the mechanism of de novo centromere formation. Using another multicellular model organism, the transparent nematode *C. elegans*, our lab discovered that foreign, naked DNA injected into the gonad of nematode can lead to fusion of injected DNA to form a chromatin-packaged artificial chromosome (AC) that is capable of replicating and accurately segregating within a few cell cycles. We identified the histone chaperone, histone modifiers and chromatin-binding proteins required for centromere formation, and we analyzed if DNA sequences play a role in determining the centromere position.

I hope that the impact of my research is not limited to these observations in these model organisms. By comparing what we learn from different organisms well separated in evolution prompts researchers to further investigate how the first eukaryotic chromosome was constructed, and how each organism evolves its chromosomes to adapt to its needs. Our results also have implications for cancer research, as

chromosome instability (CIN) is one of the underlying hallmarks of many solid cancers, but the molecular causes and consequences of it is still unclear. Centromere inactivation or new centromere formation could initiate CIN.

Q: What is your mentorship style? How have you arrived at that style, and did you use specific resources to learn or enhance your mentoring?

KY: My mentorship style is quite free and open. I value students' creative ideas and try to not make judgements too early. I try to patiently listen and provide input and guidance as students navigate [through their research]. I hope to work with students and post-doctoral fellows in lab as partners, and I encourage them to express their thoughts and feelings. I push them to strive through, and hope people in the lab are motivated and driven by their passion and curiosity to do science, instead of by pressure or to fulfil someone else's goal.

I think I inherited this free and open style from my former mentors. Both my PhD mentor Prof. Phil Hieter and postdoctoral mentor Prof. Arshad Desai are very kind, generous and open-minded. While Phil could be busy with his Director's administrative work, he still often took time to meet with us regularly. Arshad's sitting in lab and his open-door policy made it very convenient and comfortable to discuss with him.

Q: If you had not chosen centromere and chromosome research, what career would you have pursued?

KY: If I did not choose to be a molecular cell biologist, I may have pursued a career in architecture, as designing and constructing new buildings appears to be a very interesting and fascinating job. Yet, my art is not good. I'm also interested in paediatrics and genetic counselling, although the communication skills with patients could be challenging.

Q: What is the best or most helpful professional advice you have received?

KY: The best professional advice I have received is that basic, fundamental research [is important] in understanding how nature works and should precede, or at least should be done in parallel with, translational research or engineering. If there is no basic research, there is nothing to translate. Researchers can first humbly learn how nature and existing organisms tackle a problem before engineering and improving our designs, as nature may already have the best solutions awaiting for us to discover. I also remember Phil Hieter's sticker of superman yeast, labeled "the Awesome Power of Yeast Genetics". Even these days with the fast development of gene editing, I still believe that model organisms allow us to do some experiments that may not be possible in human cells. Only our imagination is the limitation.

Q: When you are not doing science what do you enjoy doing?

KY: When I'm not doing science, I enjoy reading, practising Chinese calligraphy and writing. Recently, I have written and illustrated a children story book about two brothers fighting each other, genetics, and the development of life from a single cell to an embryo through cell division. It is based on some real experience with my own two boys. The completely new endeavor has prompted me to further think how to share the wonders in life, nature, and fun in science with kids. In addition, I enjoy rock climbing. Snow and ice climbing in Yatugatake, Japan (https://www.crux.com.hk/upcomingexpedition/yatugatake-japan-snow-ice-climbing-course/) was one of the best experience in my life. I also tried climbing the 18-meter bun-covered steel tower in the traditional Hong Kong Cheung Chau Bun Festival, originally a ritual for fishing communities, but now a fun-filled carnival.