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Harnessing the Power of Whole Genome Sequencing in Analysis of Mutagenesis in Human Cells

Dr. Nik-Zainal is a CRUK Advanced Clinician Scientist and Honorary Consultant in Clinical Genetics in Cambridge, UK. Serena went to the UK as a PETRONAS scholar from Malaysia in 1993, obtaining a First in Physiology at University of Cambridge before completing her medical degree in 2000. She trained as a physician and specialized in Clinical Genetics. She undertook a PhD at the Wellcome Sanger Institute in 2009 pioneering exploration of breast cancers through whole genome sequencing (WGS).

Dr. Nik-Zainal demonstrated how detailed downstream analyses of all mutations present in WGS breast cancers could reveal mutational signatures, imprints left by mutagenic processes that have occurred through cancer development. She also identified a novel phenomenon of localised hypermutation termed 'kataegis'. Dr. Nik-Zainal continues to explore large cancer datasets using computational approaches while investigating biological underpinnings of mutational signatures through cell-based model systems. She led a clinical project, Insignia recruiting patients with DNA repair/replication defects, aging syndromes and neurodegeneration, and is also focused on advancing the field of mutational signatures into the clinical domain.

Abstract: Mutational signatures are the imprints of DNA damage and DNA repair processes that have been operative during tumorigenesis. They are biologically informative, reporting on the processes that have contributed to the developmental history of each patient's cancer. In this lecture, on behalf of my team and my collaborators, I shall provide an update on the field, focusing on validation of these abstract mathematical concepts, untangling the mechanisms underpinning mutation patterns in human somatic cells, and describing the new insights that we have gained through combinations of computational analysis and experiments in cell-based systems. We showcase how mutational-signature-based clinical algorithms have been developed, describe the path taken in translating these towards medical utility and highlight some of the hurdles that need to be navigated in this type of translational research.

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