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Editorial overview: The most difficult of years in cancer research

David J. Adams, Marcin Imielinski and C. Daniela Robles-Espinoza

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David J. Adams

Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK

Dr. Adams is a senior group leader in the Cancer Ageing and Somatic Mutation programme at the Wellcome Sanger Institute and leads the Experimental Cancer Genetics Laboratory. He is also co-head of the Cambridge Cancer Centre Cell and Molecular Biology Programme, a Fellow of the Academy of Medical Sciences, a member of the Scientific Advisory Board (SAB) of the Brain Tumour Charity, and a member of the SAB of the International Laboratory of Human Genome Research. He is also a member of the steering committee of the Society for Melanoma Research and co-leads the GenoMEL Consortium, which aims to identify genes whose mutation predisposes to melanoma development.

Marcin Imielinski[a,b]

[a] Weill Cornell Medicine, New York, United States
[b] New York Genome Center, New York, United States

Dr. Marcin Imielinski is an assistant professor of Pathology and Laboratory Medicine at Weill Cornell Medicine and Core Member at the New York Genome Center. His laboratory studies the causes and consequences of altered genome structure in cancer. As a physician-scientist and molecular genomic pathologist, he is particularly interested in the clinical applications of whole genome sequencing.

C. Daniela Robles-Espinoza[a,b]

[a] International Laboratory for Human Genome Research, National Autonomous University of Mexico, Mexico
[b] Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK

As we write this editorial overview, weary from a year of working from home, self-isolation and the turmoil that the COVID-19 pandemic has brought, we reflect on the challenges and promise of cancer research looking forward, mindful that the pandemic has changed this future in many ways, whilst also highlighting disparities in healthcare systems and access to cancer care.

In planning this edition of *Current Opinions in Genetics and Development*, we firstly wanted to provide a platform for researchers in low-and-middle income countries to tell their stories. In two reviews in this edition, the authors provide insights into cancer genomics in Sub-Saharan Africa and in Latin America, clearly illustrating their reality is very different to those of us in well-funded research powerhouses such as the US and UK. If anything positive can come from this pandemic, we hope that the cancer research community will be more global facing, realising both the challenges and opportunities for real impact in advancing access and equity, particularly in cancer genomics and new diagnostics. As the authors emphasize in their reviews the analysis of samples from non-European descent populations may provide unique biological insights that extend to all those afflicted by cancer (Alvarez-Gomez *et al.*, & Munung *et al.*).

Technology has always been a driver for advancements in cancer discovery. In this edition we have reviews discussing new technologies such as spatial transcriptomics and its application to understanding cancer ecosystems, advances in single-cell sequencing and its promise for dissecting tumour heterogeneity, and new areas of computational biology such as the analysis of allele-specific gene expression and cancer regulatory variation (Pierce *et al.*, & Hennessey *et al.*, & Maniatis *et al.* & Robles-Espinoza *et al.*). These studies provide important insights into how variation influences gene expression and cellular phenotypes, and furthers our understanding of cancer as a genetic disease. In the same way we invited authors to discuss advances in gene-editing tools in *in vivo* models of cancer, and to discuss technologies such as base-editors, CRISPRi and CRISPRa. Of note, these tools may also be used for forward genetic screens in mouse models which can inform studies of cancer gene function and also to define drivers of disease biology (van der Weyden *et al.*). Since the mouse has always been forefront in furthering our understanding of cancer, this edition also contains a review discussing advances in mouse models of colon cancer, where faithful models of the disease represent new tools for pre-clinical intervention studies (Lannagan *et al.*). An intriguing review on exosomes, which are membrane-bound extracellular vesicles that are taken up by cells and influence their behaviour (Stefanius *et al.*), is also included in this edition

Dr. Carla Daniela Robles-Espinoza is an assistant professor at the International Laboratory for Human Genome Research (LIIGH), National Autonomous University of Mexico (UNAM), and an international fellow at the Wellcome Sanger Institute, UK. She studied a BSc in genome sciences at UNAM and a PhD in cancer genetics at the University of Cambridge. Her research focuses on using large-scale sequencing data for investigating the driver alterations, risk factors and potential therapeutic targets of types of cancer important in Mexico and Latin America, such as acral lentiginous melanoma and hepatocellular carcinoma.

because they play an important role in cancer cell phenotypes but can potentially be used for cancer drug delivery.

Many of the reviews in this edition discuss insights gained from next-generation sequencing. Specifically, these technologies have driven the analysis of clonal hematopoiesis (Mitchell *et al.*), which has significant implications for our understanding of ageing and risk of blood cancers, and also our understanding of extrachromosomal DNA (ecDNA) (Wu *et al.*), which is a remarkable phenomenon that appears to influence the pathogenesis of a range of cancer types but is as yet poorly understood. In the same way, a review in this edition discusses homologous recombination and its role in generating genomic signatures (Setton *et al.*). These areas clearly have significant implications for stratifying patients and exploring disease outcomes, and are made possible by our ability to scale the analysis of the cancer genome.

No edition on cancer genomics would be complete without a discussion of therapeutic advances. Clearly, the last decade has been dominated by the advent of immunotherapy. In melanoma, renal cancer and lung cancer these agents are now standard of care, yet identifying those patients who will respond to treatment remains a significant challenge. Genomic technologies have been hugely valuable in understanding immunotherapy responses and in particular for profiling the intestinal microbiome (Cormedi *et al.*). Importantly, many studies have reported associations between specific bacterial strains and either immune-related toxicities or anti-tumour responses and genomic tools have allowed the culprits to be defined. Understanding the intestinal microbiome has also been shown to play an important role in influencing outcomes following hematopoietic stem cell transplantation, an approach widely used to treat patients with blood cancers (Nguyen *et al.*). These remarkable insights have immediate clinical implications and exemplify the translational potential of genomic analysis.

As a new year takes the reins from a difficult 2020, we cautiously yearn for a return to normal. Maybe the breathtaking speed at which COVID-19 vaccines were developed, a truly remarkable achievement and contribution to humanity, will help set the pace for a new age of cancer therapeutic development.