THE ROLE OF EMERGING BIOINFORMATIC METHODS IN IMPROVING DIAGNOSIS: A PRIMER FOR BEGINNERS

Cristin Print

Department of Molecular Medicine and Pathology, University of Auckland, Auckland, New Zealand

Next generation sequencing and related genomic methods are immensely powerful. They are transforming many clinical fields and are rapidly penetrating into pathology. However, these valuable techniques also bring with them noise and statistical uncertainty. This talk will provide a primer for beginners to the rapidly changing fields of genomics and bioinformatics, and will raise provocative issues for discussion for those already working with these technologies. The talk will aim to answer several questions: Given the complexity of genomes, can genomics and bioinformatics really provide useful diagnostic, prognostic and predictive information? How do the current genomic and bioinformatic technologies fare, and what new technologies are likely to appear in the next two years? How is the practice of bioinformatics used to interpret genomic data safely and to manage big-data uncertainty? What is the difference between targeted DNA panels and whole genome DNA analysis? Will whole genome DNA analysis, and genome-scale analysis of RNA, really be useful in clinical practice, or are these methods just research tools? How can different types of genomic and morphological data be integrated with one another to facilitate the practice of pathology? How are pathologists using bioinformatics methods in their research?

THERAPEUTIC OPPORTUNITIES FROM GENOMIC SEQUENCING

Kym M. Boycott, Alex E. Mackenzie

Children's Hospital of Eastern Ontario Research Institute, University of Ottawa, Ontario, Canada

Effective therapies for rare genetic diseases are themselves comparatively rare; there are currently 400 medicinal products on the market for rare diseases. Clinical genomic sequencing is accelerating the pace of rare disease diagnosis for patients and represents the first therapeutic opportunity as an accurate diagnosis occasionally yields an associated effective therapy. With novel gene discoveries the challenge is significant, as often the biological context of these genes is not yet well understood; however, occasionally, with new molecular insight into a given disorder, an obvious and facile therapeutic approach may present itself. Such outcomes, while exciting, are rare. Indeed, for a large number of paediatric-onset diseases, given their congenital nature and the fact that they often involve early developmental structural defects or are overwhelmingly severe, the prospect of definitive therapy is unlikely. For the remainder of disorders where there may exist a therapeutic opportunity, the diversity and number of rare diseases combined with the small numbers of patients for each disorder effectively precludes, for all but a fraction of conditions, traditional costly drug discovery approaches. This fact highlights the significant need for development of low-cost generalisable approaches for rare disease translational research going forward.

GENOME-WIDE PLASMA DNA ABERRATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

Rossa W.K. Chiu

Li Ka Shing Institute of Health Sciences and Department of Chemical Pathology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong Special Administrative Region

A pathognomonic feature of systemic lupus erythematosus (SLE) is the presence of anti-dsDNA antibodies. Because cell-free DNA is present in human plasma, we asked if the presence of anti-dsDNA antibodies is associated with plasma DNA aberrations of SLE patients. Interestingly, we have observed a number of aberrant features among the plasma DNA molecules of SLE patients. Distribution of plasma DNA molecules across the genome could be affected. The size profiles of the plasma DNA molecules are altered. The methylation profile of the plasma DNA molecules could also be different. On one hand, such features may confound the findings of patients undergoing non-invasive prenatal testing or liquid biopsy for cancer assessment. On the other hand, further studies could be designed to address the potential utilities of plasma DNA analysis for the investigation of SLE.

Acknowledgement: Supported by the Research Grants Council of the Hong Kong SAR Government under the Theme-based research scheme (T12-404/11).

NON-INVASIVE PRENATAL TESTING: WHAT'S NEXT?

Rossa W.K. Chiu

Li Ka Shing Institute of Health Sciences and Department of Chemical Pathology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong Special Administrative Region

Non-invasive prenatal testing (NIPT) by cell-free fetal DNA analysis in maternal plasma has been clinically adopted for fetal chromosomal aneuploidy screening in many programmes worldwide. Maternal plasma comprises a background of maternal DNA and the lesser portion, fetal DNA, which is predominantly derived from the placenta. Consequent to the large volume of tests performed, the NIPT results are providing us with a renewed understanding of maternal and placental physiology or pathology. Some of these circumstances would result in what would be considered as false-positive or false-negative findings. On the other hand, developments in NIPT technologies might allow the detection of fetal monogenic diseases, subchromosomal aberrations, and other non-genetic conditions. With improvements in single-molecule sequencing, point-of-care NIPT might even be possible.

Acknowledgement: Supported by the Research Grants Council of the Hong Kong SAR Government under the Theme-based research scheme (T12-403/15-N).

IRDiRC AND GA4GH: INTERNATIONAL EFFORTS TO ADVANCE RARE DISEASE DISCOVERY

Kym M. Boycott¹, on behalf of IRDiRC* and GA4GH**

¹*Children's Hospital of Eastern Ontario Research Institute, University of Ottawa, Ontario, Canada; *www.irdirc.org*

^{**}*www.genomicsandhealth.org*