NON-INVASIVE PRENATAL TESTING (NIPT) IS MORE SENSITIVE THAN CVS FOR IDENTIFYING RARE TRISOMY AND TRISOMY MOSAICISM

Nicola Flowers, Olivia Giouzeppos, Sara Cronin, Grace Shi, David Francis, Damien Bruno, Mark Pertile
Victorian Clinical Genetics Services, Murdoch Childrens Research Institute, Royal Children's Hospital, Melbourne, Vic, Australia

Aim: Low coverage (0.2x) whole genome sequencing data obtained from non-invasive prenatal testing (NIPT) can be used to identify trisomies other than 13, 18 and 21. We compared the frequency of 'off-target' trisomies identified by NIPT with that of non-standard trisomies reported in the CVS literature.

Methods: Normalised chromosome coverage data were examined in 6,000 consecutive NIPT referrals to identify 'off-target' trisomies. Cases suspected of trisomy underwent additional aneuploidy assessment using WISECONDOR.¹

Results: 'Off-target' trisomies were identified in 42/6,000 (0.7%) NIPT referrals. Several cases were associated with miscarriage (trisomy 15,22), true fetal mosaicism (trisomy 2,7,16,22), or uniparental disomy (UPD) following trisomy rescue (chromosomes 2,15). Trisomy 7 (8 cases) was the most frequently observed non-standard trisomy, which is concordant with the CVS literature.

Discussion: These data demonstrate the clinical utility of NIPT for identifying rare trisomy and trisomy mosaicism. Although the majority of findings likely represent confined placental mosaicism (CPM), we have confirmed rare trisomies in miscarriage tissue and at amniocentesis. A pregnancy with maternal UPD15 associated with Prader-Willi syndrome was also identified. The increased frequency of 'off-target' trisomies identified by NIPT (0.7%) when compared with the CVS literature (0.32%) suggests a greater sensitivity for detecting placental trisomy and trisomy mosaicism.

Reference

1. Straver R, Siermans EA, Holstege H, *et al.* WISECONDOR: detection of fetal aberrations from shallow sequencing maternal plasma based on a within-sample comparison scheme. *Nucleic Acids Res* 2014; 42: e31.

QUALITY ASSURANCE PROGRAM REVIEW FOR SOMATIC CANCER MODULES

Kumari Hallwirth Pillay, Sze Chai, Kwang Hong Tay, Nalishia Pillay, John Christodoulou
RCPAQAP Molecular Genetics, St Leonards, NSW, Australia

The RCPAQAP Molecular Genetics Discipline offers quality assurance modules in the Australasian region for the molecular genetic analysis of inherited and somatic diseases.

The discipline has expanded the scope of quality assurance modules and participation in these modules has steadily increased over the last three years to >30 for some oncology modules. This report presents the survey outcomes for the Oncology Program, which includes the EGFR, KRAS and BRAF modules. The outcomes of a NRAS pilot module, which was established in 2014 will also be discussed.

The EGFR, KRAS and BRAF modules were NATA accredited in 2013. The modules were designed to assess laboratory

performance in the detection of genetic mutations from patient-derived formalin-fixed paraffin-embedded (FFPE) tumour tissue samples, together with interpretive comments provided to the referring clinician.

In 2016, multigene modules for Lung Cancer, Colorectal Cancer and Melanoma will be introduced and laboratories will be given the opportunity to incorporate several genes into their testing and analysis.

An overview of the results obtained, methods employed and areas for improvement will be presented.

The RCPAQAP would like to acknowledge the Australian Government, Department of Health Quality use of Pathology Program (QUPP) for their funding assistance in this project.

MOLECULAR GENETICS QA SAMPLE EXCHANGE PROGRAM

Kumari Hallwirth Pillay, Kwang Hong Tay, Sze Chai, Nalishia Pillay, John Christodoulou
RCPAQAP Molecular Genetics, St Leonards, NSW, Australia

The RCPAQAP Molecular Genetics Discipline established a sample exchange program, which was designed to assist laboratories in periodically monitoring the accuracy of their results from molecular genetics assays for rare, infrequently tested genes or where there is no established QAP.

This project was undertaken during the course of 2014 and 2015. In 2014, 16 modules were offered and 15 in 2015. Samples were donated to the QAP and they were subsequently dispatched to laboratories in a blinded format.

The following sample exchanges were produced: ALK translocation in NSCLC, CDH1 genotyping, coeliac disease, CYP2C9, CYP2C19, IDH1/IDH2 sequencing, IL28B genotyping, Kennedy's disease, MGMT hypermethylation, MLH1 promoter methylation, oligodendroglioma LOH 1p19q, PTEN genotyping, SDHB genotyping, TP53 genotyping, TPMT genotyping and Von Hippel Lindau syndrome. The ALK translocation in NSCLC sample exchange was converted into a pilot Quality Assurance module in 2015 owing to increased demand and positive feedback.

Following analysis, concordance reports were generated. These included methods performed and publications utilised for interpretative comments. An overview of the results will be presented together with discussions on key modules.

Acknowledgement: The RCPAQAP would like to acknowledge the Australian Government, Department of Health, Quality use of Pathology Program (QUPP) for their funding assistance in this project.

INTRINSIC FACTORS DO NOT CAUSE OVEREXPRESSION OF POLO-LIKE KINASE 1 (PLK1) IN COLORECTAL CANCER (CRC)

Wayne Ng^{1,2}, Joo-Shik Shin^{1,2,3}, Bin Wang^{1,4}, Cheok Soon Lee^{1,2,3}

¹Discipline of Pathology, Western Sydney University, ²Cancer Pathology and Cell Biology Laboratory, Ingham Institute for Applied Medical Research, ³Molecular Medicine Research Group, School of Medicine, Western Sydney University, and