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Comprehensive genomic profiling (CGP) describes technologies that allow profiling of all major types of genomic alterations, including simple nucleotide variation (SNV and indel), somatic copy number alteration (SCNA), structural variation (SV), and aggregate markers of genome damage such as tumour mutation burden (TMB) and microsatellite instability (MSI). CGP could lead to improved access to molecularly targeted therapies for cancer patients but, aside from a few accredited commercial and academic providers, is not widely used in routine pathology practice. Aspects of CGP presenting barriers to broad adoption include cost, technical complexity, lack of reimbursement, and a perceived lack of clinical utility. Here we summarise the experience of Peter Mac's Pathology Department in providing CGP in the translation research setting over three years of testing for personalised medicine trials. We find that characterising tumours using a comprehensive in-house clinical research panel provides useful diagnostic and predictive information that impacts patient care in a number of cases, however at relatively high per sample cost. In comparison, we describe our experience with one of the first kit-based CGP research products on the Australian market meeting the requirements for routine CGP.

IMPROVING GENOMICS AND BIOINFORMATICS LITERACY IN THE UNDERGRADUATE MEDICAL SCIENCE CURRICULUM

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Background: The growth of genetic sequencing requests for pathology diagnoses and personalised medicine demands that graduating medical scientists be cognisant of genomics and bioinformatics, in preparation for their future careers.

Aim: To improve the genomic and bioinformatics literacy of undergraduate Medical Science students.

Methods: QUT Bachelor of Medical Science students enrolled in a fourth-year core unit, studied a series of lectures and workshops covering genomic and bioinformatics analysis of bacterial, human germline and somatic case studies relevant to pathology diagnosis. The bioinformatics platform used was Galaxy. Students voluntarily and anonymously completed a survey prior and subsequent to the workshops to ascertain their growth in genomic literacy.

Results: Fifty-five students completed the pre-workshops survey: eight students declared 'very little' prior experience with bioinformatics, and four declared some experience in coding. The other students declared no previous experience. Fifteen students completed the post-workshop survey, of which 14 were 'a bit confident' or 'moderately confident' in their abilities. Eight students were moderately or strongly interested in continuing study in this area.

Discussion: Embedding and advancing teaching and learning of clinical genomics and bioinformatics in the undergraduate Medical Science curriculum is crucial for providing career-ready graduates in this burgeoning discipline of pathology.

URINE ORGANIC ACID (UOA) ANALYSIS FOR THE DIAGNOSIS OF AROMATIC L-AMINO ACID DECARBOXYLASE (AADC) DEFICIENCY

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We describe the use of urine organic acid (UOA) analysis for the diagnosis of a CSF neurotransmitter defect, aromatic L-amino acid decarboxylase (AADC) deficiency in a 3-month-old boy. The patient presented with upper limbs spasm and abnormal eye movement. UOA was initiated for possible inborn errors of metabolism (IEM). Hyper-excretion of urine vanillic acid (VLA) and N-acetyl-vanilalanine was detected in UOA which the pattern is pathognomonic to AADC deficiency. The diagnosis was subsequently confirmed by analysing the hotspot pathogenic variant in the *DDC* gene, i.e., IVS6+4A>T in <2 days. A CSF neurotransmitter profile was requested by the clinician and showed a classical pattern of AADC deficiency with markedly elevated 3-O-methyldopa of 2895 nmol/L (RI <300) and very low levels of 5-HIAA (<17 nmol/L; RI 114–335) and HVA (<67 nmol/L; RI 295–932). Because CSF sampling can be technically challenging and is also invasive, our case illustrates the potential of using non-invasive UOA to replace CSF neurotransmitter for the diagnosis of AADC. This is particularly useful clinically if sampling of CSF is practically infeasible. In conclusion, UOA is a simple and non-invasive test for AADC deficiency, and substantiate the previous work reported by Lee *et al.*¹

Reference

1. Lee HC, Lai CK, Yau KC, *et al.* Non-invasive urinary screening for aromatic L-amino acid decarboxylase deficiency in high-prevalence areas: a pilot study. *Clin Chim Acta* 2012; 413: 126–30.

IMPACT OF MATERNAL EXERCISE ON THE FRACTION OF FETAL CELL FREE DNA IN MATERNAL PLASMA

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Aim: Maternal exercise prior to non-invasive prenatal testing (NIPT) may reduce the fraction of cell free DNA attributable to the fetus ('fetal fraction'), a key determinant of NIPT performance. This pilot study aimed to assess the impact of maternal exercise on fetal fraction.

Methods: 15 pregnant women of gestational age ≥ 10 weeks were recruited from a public hospital antenatal service. Moderate exercise was undertaken (clinical exercise stress test as per Bruce protocol with target heart rate of 140 bpm), with peripheral blood collected pre- and post-exercise. Gestational age, maternal age, maternal body mass index (BMI), heart rate, and blood pressure were recorded. Fetal fraction was determined by the Harmony NIPT assay.