



Dear Colleagues,

Welcome to the Dec 2014 (Issue 6) update of POLARIS! Supported by A\*STARs SPF scheme, POLARIS is now just reaching the two year old mark. Since our last update in July, our team has continually focused on our core mission of translating and implementing promising local genomic research findings back to Singapore patients.

### ***POLARIS BIM assay – our second clinical test!***

We are pleased to announce the completion of our 2<sup>nd</sup> clinical implementation test. The POLARIS BIM assay is a Sanger-based assay designed to detect germline genetic deletions in the *BIM* oncogene. This test is based on research work led by A/Prof Ong

Sin Tiong from Duke-NUS, and a multi-disciplinary team from Duke-NUS, GIS, SGH, and NCCS. In a seminal paper, A/Prof Ong's team discovered that cancer patients with this *BIM* deletion polymorphism, which is only present in the Asian population, exhibited inferior clinical responses to a variety of targeted therapies (Ng et al., 2012 *Nature Medicine*). The POLARIS *BIM* polymorphism test is now available at SGH, and investigators at NCCS are now using the availability of this clinically-certified test, which is the first in the world, as an incentive to pharmaceutical industries to conduct clinical trials targeting patients with the *BIM* deletion genotype. A/Prof Ong said "Since our original publication, investigators from Japan, Taiwan, and China have independently validated our work. That POLARIS has made this test available in a clinical context will now allow physicians to predict how long patients are likely to benefit from expensive targeted therapies. Importantly, this test will in the near future also help physicians select patients for inclusion in clinical trials testing new therapies to overcome resistance conferred by the *BIM* deletion."

### ***POLARIS Lab Infrastructure – Enabling Clinical Next-generation Sequencing (NGS)***

Progress continues on one of POLARIS's core objectives, which is to obtain CAP (College of American Pathologists)-accreditation for the POLARIS@GIS and POLARIS@SingHealth facilities in 2015. As part of the accreditation requirements, the POLARIS@GIS laboratory is currently undergoing a series of Proficiency Testing (PT) exercises. As background, accredited laboratories must demonstrate that they have the ability to consistently provide accurate diagnosis of patient samples. PT assesses the ability of the laboratory to process and diagnose unknown samples, and the laboratory is graded on how accurately it performed the testing. After the test, the laboratory will be informed how well it has done relative to other laboratories participating in the same PT panel. POLARIS has obtained approval from CAP to conduct its PT by subscribing to molecular panels provided by the UK NEQAS (United Kingdom National External Quality Assessment Service). To date, the POLARIS@GIS lab has completed 2 rounds of PT. For the first round, we passed with a score of 93%. The PT exercises have proved invaluable in identifying opportunities for improving our workflows, covering diverse activities ranging from sample handling, NGS library construction, and results reporting.

In parallel to the POLARIS@GIS laboratory, the POLARIS@SingHealth lab has also been set up and is undergoing exercises for accreditation. Of note, we are pleased to announce that samples can be tracked and monitored by both SGH and GIS using the same Laboratory Information Management System. This will facilitate transfer of new protocols and tests between the two Polaris lab sites, and systematic review and improvement between both sites. Our Polaris Clinical Director, Dr. Tony Lim, can review clinical reports at both the SGH and GIS Polaris lab sites. The improved communication will promote synergistic interactions between GIS and SGH.

### ***New POLARIS Core Team Member - Alexander Lezhava***

We are pleased to welcome Dr Alexander "Sandro" Lezhava as a new member of the POLARIS Core Leadership Team. Currently, Sandro leads the Translational Research Group at GIS. Prior to GIS, he was Research Director at the Singapore-based company Dx Assays, and spent >10 years as a unit leader at the

Omics Science Center, RIKEN Yokohama Institute. At GIS, Sandro's team will work on developing molecular diagnostics for personalized patient care, leveraging on the POLARIS infrastructure and also the newly established GIS Molecular Diagnostics Laboratory, a shared facility which has been designed and constructed in compliance to ISO 13485 standards for sample preparation and analysis activities. Sandro's wealth of experience will greatly facilitate the mission of POLARIS which is to translate local bio-marker discoveries into clinically-validated and implementable assays. Welcome Sandro!



*Dr Sandro  
Lezhava, new  
Core Member of  
POLARIS*

### ***POLARIS in Academia –OMIC Approaches to Clinical Medicine***

Research projects supported by POLARIS are now beginning to reach academic fruition. Over the past 6 months, POLARIS investigators, in collaboration with teams from GIS, TTSH, MOH, NUS (SSHSPH), and SGH, have published a paper describing the use of pathogen NGS to track outbreaks of tuberculosis (“MDR-TB outbreak in LAN gaming centers”), currently in press at *Emerging Infectious Diseases*, a flagship journal of the US Centers for Disease Control and Prevention (CDC). One of the investigators, Dr Hsu Li Yang, opines that “Next generation sequencing is currently the most discriminatory molecular tool for defining the epidemiology of Mycobacterium tuberculosis, and is potentially a critical asset for determining transmission chains and hence contact tracing of TB patients. It also has great potential for the rapid determination of drug resistance for TB, and will undoubtedly play an important role in TB treatment in the near future.” We wish to acknowledge support from MOH to the participating hospitals for this project.

The POLARIS program was also orally presented at the recent American Society for Human Genetics meeting in San Diego (Oct, 2014), under a “Clinical Cancer Genome” session organized by the Global Alliance for Genomics and Health (GA4GH), an international consortium of academic, clinical, and industry partners working on the clinical implementation of genomics. The POLARIS presentation, delivered by Prof Teh Bin Tean of NCCS, was bookended by similar presentations from Charles Sawyers and Mark Lawler that described related efforts in Europe and North America.

### ***POLARIS Community Outreach and Meetings***

POLARIS is continuing its efforts to arrive at local community standards for the clinical implementation of genomics. As part of this effort, POLARIS has hosted additional community sessions to educate clinicians and researchers on the use of genomics in the clinic. The most recent POLARIS CME-accredited community meeting was held on 4th Nov 2014 at two sites, SingHealth and KKH, in collaboration with Illumina. The first session was held at Academia and titled “Precision Oncology”, presented by Dr Daniel Grosu, Vice President of Clinical Development at Illumina. This session was attended by over 40 oncology clinicians and researchers and hosted by Dr Iain Tan (NCCS). Dr. Grosu reviewed cancer mutation driver genes and the role of NGS for detection of cancer cell subtypes for treatment-focused interventions. He also discussed the emerging utility of liquid biopsies to collect circulating tumour DNA in blood or urine for early cancer detection and monitoring as well as discovery of treatment-resistant mutations. The second education session was a clinical genomics lunchtime seminar held at KKH. Dr. Maggie Brett (KK Research Centre) presented the experience of applying chromosomal microarray analysis and exome sequencing for the provision of a molecular diagnosis in a clinical paediatric setting. Dr. Grosu followed with an overview of the clinical application and progress of NGS in non-invasive prenatal testing, prenatal genetic screening and diagnosis, rare inherited diseases and oncology. This session was kindly hosted by Dr Saumya Shekhar and very well attended by paediatric, obstetrics and gynaecology clinicians and diagnostic laboratory scientists at KKH.

Best wishes for the Holiday Season!  
Patrick Tan  
(On behalf of the POLARIS Team)



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