Recent Achievements

Our Postdoc Oscar Torres and PhD student Sarah Buddle presented at the Oxford Nanopore Technologies London Calling Conference in May.

1 Sarah shares her insightful experience

Oscar and I attended the Oxford Nanopore Technologies London Calling Conference in May. Oscar gave a short talk and presented a poster on our work on adeno-associated virus hepatitis, and I showed a poster of our work comparing metagenomics methodologies for detection of viruses in high human background samples. It was great to discuss this work with lots of people who were using or setting up metagenomics in many different contexts, including diagnostics and public health. There were also some interesting talks from people using ONT in infectious diseases, including for tracking outbreaks and surveillance for emerging pathogens.

Link to the video: https://youtu.be/kjffMFfVOVc?si=fJLv-9WbPY37uwW3

Summary of the research

Evaluating metagenomics and targeted approaches for diagnosis and surveillance of viruses

Background:

Metagenomics is an advanced method for detecting unknown and new pathogens. Illumina short-read sequencing is becoming common in labs for this purpose, but it requires a lot of sequencing, takes a long time, and isn't very sensitive. Newer methods using Oxford Nanopore Technologies (ONT) allow real-time data analysis, potentially needing less sequencing and enabling quick testing right at the point of care. Targeted methods that focus on known pathogens can also improve sensitivity.

Methods:

We tested virus detection using untargeted metagenomics with Illumina and ONT, and a targeted Illumina approach using the Twist Biosciences Comprehensive Viral Research Panel (VRP), which focuses on 3153 viruses. We used a mixture of six viruses in a human DNA/RNA background to simulate clinical samples with low levels of microbes and high levels of human genetic material. We kept the host genetic material to help confirm if there were no infectious agents.

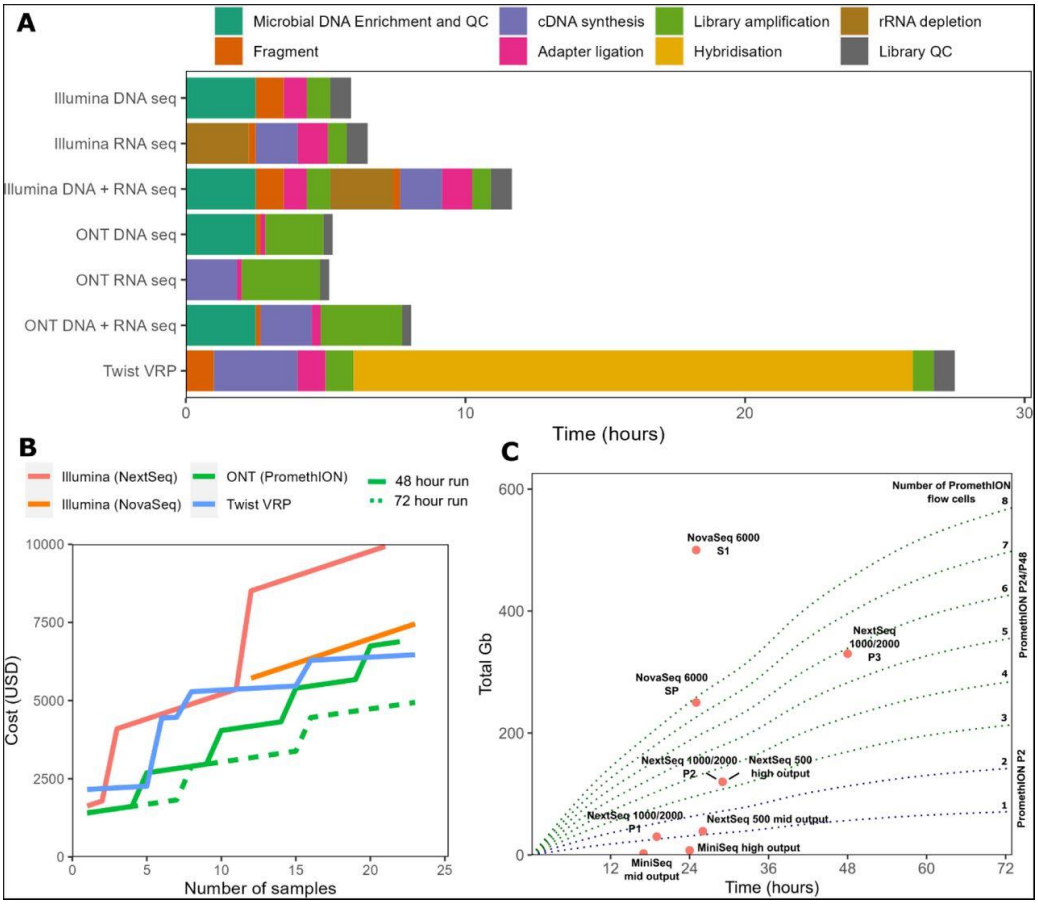
We also compared how well different taxonomic classifiers performed.

Results:

The Twist VRP increased sensitivity by 10-100 times compared to untargeted sequencing, making it good for detecting low viral loads (60 genome copies per milliliter). However, other methods might be needed to find unknown organisms in a diagnostic setting. ONT was good at detecting high viral loads (60,000 genome copies per milliliter) but needed longer and more expensive sequencing runs for lower viral loads (600-6,000 genome copies per milliliter) to match Illumina's sensitivity. ONT provided better specificity than untargeted Illumina sequencing. Standard thresholds helped make results from different taxonomic classifiers consistent. Host gene expression analysis was best with untargeted Illumina sequencing but possible with both VRP and ONT.

Conclusions:

Metagenomics could become a standard method in diagnostics and is very useful for discovering new pathogens. Untargeted Illumina and ONT metagenomics and the targeted Twist VRP each have unique benefits in terms of sensitivity, specificity, turnaround time, and cost. The best method to use will depend on the specific clinical situation.



Turnaround times and output data volumes

A Time taken for library preparation for the different protocols tested. The Twist panel uses a combined DNA and RNA-Seq protocol. The DNA+RNA bars for the untargeted sequencing indicate the time taken if both protocols are performed by a single operator. B Total cost (including library preparation) to sequence number of samples indicated plus single negative control, to a depth of 5GB. ONT costs are shown with 48- and 72-hour maximum run times per flow cell. C Volume of data output by time for a range of Illumina sequencing kits and ONT sequencing with PromethION flow cells. The Illumina kits produce a set amount of data after the sequencing run is complete – this is shown by pink dots. In ONT sequencing, data is output continuously and the run can be stopped at any time, until the flow cell becomes degraded. PromethION data (green/blue dotted lines) shows the average of our RNA and DNA-Seq runs, passed reads only. Data outputs for Illumina were obtained from the product specification data as of April 2024.

Recent events

2nd Genomics Workshop: NHSBT & BTRU GEMS

On April 25, 2024, NHSBT Filton successfully hosted the second Genomics Workshop, which was attended by over 50 researchers and representatives from NHSBT and GEMS. The meeting aimed to unite researchers to share data, best practices, and foster innovation and discussion across themes. Dave Roberts, Medical Director for Pathology, presented on the benefits of matching red blood cells (RBC) for kidney transplant recipients, using a technique called 'HLA-typing' (a process used to match patients and donors). Jennifer Martin, an external speaker, discussed the use of nanopore sequencing in RBC typing. Judy Breuer, Theme 2 lead at GEMS, presented on optimising metagenomics for encephalitis and other applications. Tim Sprosen, Executive Director of Participant Recruitment Operations at Our Future Health, shared insights and future developments of Our Future Health applications.

In parallel workshops on future possibilities, Workshop I focused on a study combining HLA typing, RBC typing, and Microbiology for organ donor screening, emphasising the need for IT infrastructure, cautious method integration, technology consideration, and evaluating changes before implementing new processes. Workshop II addressed bacterial genomics and NHSBT needs, highlighting the necessity of good Laboratory information management system, electronic systems, logistic challenges, and research expertise. Workshop III discussed lessons from microarray for HLA typing, stressing technology, data integrity, regulatory requirements, sustainability, responsiveness to infections, industry partnerships, and guidance for achieving CE (European Conformity) marking.

Source: https://www.pbsc.co.uk/case-studies/nhs-blood-and-transplant-facility-filton/

Public engagement and involvement

Pride month June 2024

For the first time, we collaborated with the Medical Sciences Division of the University of Oxford to organise this event. In 2021, a landmark policy change in blood donation was implemented in the UK, making the donation process more inclusive for gay and bisexual men. In this talk, Katy Davison from the UK Health Security Agency shared insights on monitoring the outcomes of these policy changes. Additionally, Jaid Debrah, a PhD student at Radcliffe Department of Medicine, presented her work on evaluating the impacts of the new policies.

Biomedical Research Centre Open Day, May 2024

On 28 May, researchers headed to the Westgate Shopping Centre in Oxford for an engaging day filled with blood safety-related activities, including making DNA code bracelets and "fishing" for DNA magnets in a vat of fake blood. Through these activities, our researchers shared their experiences of research with members of the public.

Shannah, one of our postdocs, remarked: "I really loved how much the younger children enjoyed the interactivity of the activities. Although the activities were aimed at younger children, they were also a fantastic way to visually demonstrate to older children and adults how targeted metagenomic sequencing works and what we're trying to achieve with it. I also enjoyed talking to the students about careers in science. It was a great day!"

Rich, another postdoc, shared: "I had great fun meeting with the general public over a giant bucket of fake blood. I was expecting the exercise to be most popular with young kids, but we had great engagement from teenagers and adults too. Hopefully, we inspired a few aspiring scientists to consider a career in medicine!"

Policy engagement event

A well-attended meeting for World Blood Donor Day, Su Brailsford and Heli Harvala explored the vital intersection of maintaining blood safety and promoting inclusivity within the NHS Blood and Transplant service. Dr. Brailsford discussed her instrumental role in the 'For the Individual Assessment of Risk' (FAIR) Steering Group. We discovered how this initiative enhanced equality in donor selection, especially concerning sexuality, sexual behaviour, and minority ethnic communities, whilst ensuring the highest standards of blood safety. Dr. Harvala shared her cutting-edge research on Occult Hepatitis B infection in blood donations. We learnt about her work in implementing advanced screening methods introduced last year to effectively manage this risk. The event was funded by OPEN (Oxford Policy Engagement Network) and organised by BTRU-GEMS.

To look forward to ...

Some of our upcoming events

10-11 September 2024
BTRU-GEMS Annual Meeting, Pembroke College

26 October 2024
Ideas festival: science, ideas and creative activities for everyone, location TBC