Recent Achievements

LAY SUMMARY

INTRODUCING CASTANET: *new software to enhance our ability to detect viruses and bacteria in blood donations more effectively*

By Rich Mayne

How do we currently detect viruses and bacteria in blood donations?
Our current blood and organ screening is very effective and involves checking each donation for genetic material (DNA and RNA) from specific microorganisms that we know can cause harm, e.g. hepatitis C. We currently routinely test for six different viruses and bacteria in blood donations, with more testing if necessary (e.g. based on donor's travel history).

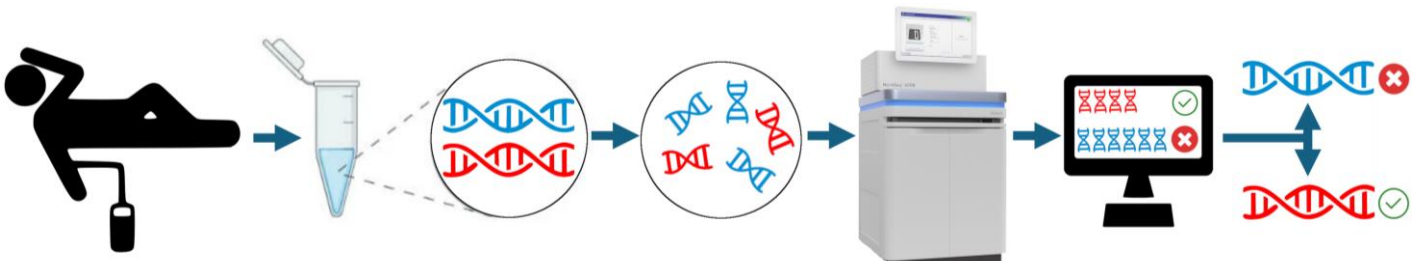
Find out more at my talk on day 2 of the Annual Meeting, at midday! Or find me in the coffee break

How are GEMS aiming to improve blood safety?
The GEMS team advocates for more extensive screening using a newer technology, next generation sequencing (NGS). NGS allows us to test for more microorganisms in one go, by examining all of the genetic material in a blood sample. This method is like a fishing net that can grab everything of interest to us, all at once – whereas the current screening method is akin to a fishing rod, searching for specific viruses one-by-one. Benefits of NGS include detection of new (emerging) infectious microorganisms, helping us work out if disallowed donors are in fact safe (e.g. if they have travelled to areas with endemic diseases) and providing additional information to the NHS about donor health.

Next-generation sequencing (NGS) is a modern technology that allows scientists to read the genetic code of an organism in a quick and cost-effective manner

What is Castanet?
Castanet (as in "cast a net" for "fishing out" genetic material) is our software for cleaning, assembling and analysing NGS data as an all-in-one tool. It was designed to be quick and simple to use, and is "open source" software, which means that anyone is allowed to download and use it for free.

How does Castanet improve blood screening?



1 We receive a blood donation

2 We extract <u>all</u> of the genetic material in the blood sample

3 We break the DNA into tiny chunks

4 Each 'chunk' is read by a special machine

5 Castanet software figures out which 'chunk' belongs to which microorganism

6 This information helps filter out infectious from non-infectious donations

An expert summary of Castanet is provided on the next page

Recent Achievements

EXPERT SUMMARY

INTRODUCING CASTANET

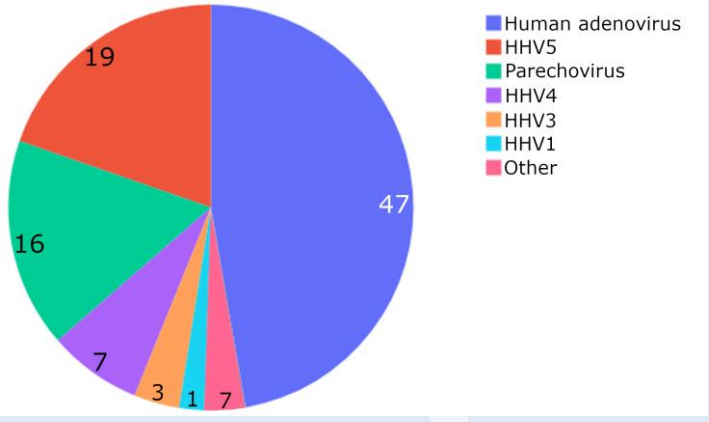
A freely-available, end-to-end pipeline for multi-pathogen sequencing data

Read the pre-print here ▸

By Rich Mayne | ORCID: 0000-0003-1915-4993

Target enrichment strategies generate genomic data from multiple pathogens in a single process, greatly improving sensitivity over metagenomic sequencing and enabling cost-effective, high throughput surveillance and clinical applications. However, uptake by research and clinical laboratories is constrained by an absence of computational tools that are specifically designed for the analysis of multi-pathogen enrichment sequence data. Here we present the Castanet pipeline: an analysis pipeline for end-to-end processing and consensus sequence generation for use with multi-pathogen enrichment sequencing data. Castanet is designed to work with short-read data produced by existing targeted enrichment strategies, but can be readily deployed on any BAM file generated by another methodology. It is packaged with usability features, including graphical interface and installer script.

In addition to genome reconstruction, Castanet reports method-specific metrics that enable quantification of capture efficiency, estimation of pathogen load, differentiation of low-level positives from contamination, and assessment of sequencing quality. Castanet can be used as a traditional end-to-end pipeline for consensus generation, but its strength lies in the ability to process a flexible, pre-defined set of pathogens of interest directly from multi-pathogen enrichment experiments. In our tests, Castanet consensus sequences were accurate reconstructions of reference sequences, including in instances where multiple strains of the same pathogen were present. Castanet performs effectively on standard laptop computers and can process the entire output of a 96-sample enrichment sequencing run (50M reads) using a single batch process command, in < 2 h.



Castanet in action

Example Castanet output graph showing approximate read distribution in a sample. Numbers represent percentage of mapped reads in the sample.

Get started with Castanet!

1.Castanet requires a bash-like environment and is tested on Ubuntu 22.04, Windows Subsystems Linux and Mac OS.

2.Navigate to the software repository and download/clone the code https://github.com/MultipathogenGenomics/castanet

3.Follow the installation instructions in the readme, found at the download link.

4.Source a mapping reference (multi-FASTA) to correspond to your capture probes.

5.A simple run can be triggered with the command provided*, where arguments are (a) your input data directory (.fastq.gz read pair); (b) experiment name; (c) output folder name, (d) mapping reference

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*Command to insert:$ python3 -m dev.castanet_lite -ExpDir <a> -ExpName <b> -SaveDir <c> -RefStem <d>

STORIES FROM OUR PATIENT AND PUBLIC CONTRIBUTORS

Firoza

For our first newsletter patient interview, we spoke with Firoza to learn about what drew her to public involvement and GEMS research

Hi Firoza, tell us about yourself and your transplant journey
Hello, I'm Firoza. I'm a 46-year-old South Asian woman living in Leicester. I'm a florist by trade, but unfortunately I had to stop working due to my physical health conditions. I also have mental health conditions and I'm neurodiverse. I'm a mother and I live with various conditions including glaucoma. Following multiple eye surgeries I had to have a Baerveldt tube fitted about nine years ago, and a corneal transplant at the same time to cover it.

Why did you want to be involved in GEMS research?
I wanted to be a blood donor, but I can't due to my transplant – so I want to help in other ways.

Why is it important for you to be involved in GEMS research?
It's important, as, in my experience, not many non-white people are involved in research. I hope to be a voice to those who cannot speak for themselves and also to represent the community that's hard to engage with

What have you enjoyed about other PPI experiences that you've had?
The thing I've enjoyed the most is presenting at conferences, even though it's scary and I do get anxious.

Tell us about your hobbies
I enjoy baking, and my favourite cake is lemon drizzle

Steve

Steve, a former biomedical scientist, turned GEMS PPI committee member, tells us his story ...

Working in a hospital laboratory you are trained to be cautious with blood. Hepatitis vaccination is mandatory. Blood samples are placed in sealed bags and only handled wearing protective gloves. Accidental blood injection is treated as a serious due to the risk of infection.

When I found out I was having chemotherapy for cancer I knew that there was a strong possibility I would become anaemic and require a blood transfusion. I was very apprehensive about receiving blood from an unknown source. My mission was to try everything possible to improve my blood count through diet – spinach, dried fruits and even liver!! (I still cannot eat liver).

After weeks of chemotherapy my efforts were futile and my blood was so depleted I needed a few units of blood. Despite my apprehension there was no real option and I waited to see the consequence. I actually felt a bit better! I didn't have any reaction or develop any infection – or inherit the personality of my donor – or acquire any new diseases!

Working with the Genomics to Improve Microbial Screening project has opened my eyes to the many issues around providing blood, blood products and transplantation with care and precision. Advances in science, especially molecular testing, is providing the opportunity to reduce risk of microbial infection from donated biological material. There is also the possibility of detecting new and emerging disease in the UK.

Jargon-busting wordsearch

Science can be puzzling sometimes. BTRU-GEMS scientists have shared key words for their research and their meanings for this Annual Meeting-themed wordsearch

COMPETITION TIME! 🏆 SUBMIT YOUR COMPLETED WORDSEARCH BY NOON ON DAY 2, IN THE STEINWAY ROOM

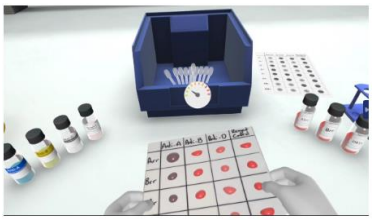
Name .....

A	B	I	S	I	T	I	T	A	P	E	H	G	W	U	G	M	D	J	B	K	X	R
G	S	H	W	F	K	D	I	Q	A	Y	H	Q	K	L	C	O	F	A	S	I	L	E
P	Y	V	J	G	A	R	D	K	X	D	Z	E	M	E	R	G	I	N	G	E	A	E
G	L	Z	X	I	S	X	I	Q	J	E	I	D	A	J	T	F	T	R	B	H	G	B
O	P	A	H	C	Z	S	T	V	Z	O	K	M	X	L	Z	B	A	I	H	X	V	H
Q	Z	A	L	P	P	U	O	Q	P	Y	A	I	V	E	D	D	E	D	R	V	A	O
P	C	R	A	Y	S	E	S	U	R	I	V	O	L	L	E	N	A	B	S	S	X	A
D	T	A	V	R	E	X	K	O	J	X	A	P	R	U	Q	B	P	Y	C	K	Z	R
E	N	A	V	S	U	R	I	V	S	E	P	R	E	H	K	L	O	V	R	P	D	H
V	P	J	G	D	Q	R	D	U	J	V	A	K	Z	F	O	Z	A	J	E	R	E	I
N	L	A	R	R	E	F	E	D	G	P	Y	Y	S	G	N	U	C	M	E	G	M	P
B	I	O	M	A	R	K	E	R	R	I	T	P	L	X	F	V	Z	L	N	P	O	X
R	O	K	D	Q	F	I	S	U	I	S	C	A	S	T	A	N	E	T	I	D	R	U
M	I	B	T	R	U	T	U	I	P	I	P	E	L	I	N	E	Y	F	N	H	I	B
C	K	Q	L	X	M	I	C	R	O	O	R	G	A	N	I	S	M	Y	G	T	V	H
Y	O	M	Z	F	U	E	P	I	M	L	H	Q	H	K	K	T	D	Y	I	W	T	P

- ❑ **Microorganism**: a microorganism (or microbe) is a tiny, usually single-celled organism. They are found almost everywhere on Earth, including in our blood and tissues. They include bacteria, archaea, fungi, protozoa, algae, and viruses.
- ❑ **Virome**: the collection of viruses that are found in the human body, including those that exist in human cells and those that infect the microorganisms within us.
- ❑ **Anelloviruses**: a family of small viruses that consist of a single strand of circular DNA and are found in the blood of most healthy people. They form the major component of the human virome.
- ❑ **Emerging**: emerging infectious diseases are infections that have recently appeared within a population (e.g. the UK) or those whose which threaten to appear in the near future.

Don't miss!

Check out our virtual reality experience : learn how to find the right blood match for transfusion in the STEINWAY ROOM



To look forward to ..

Upcoming events

26 October 2024, 10-17
Science Oxford Centre
Ideas Festival, Live Lab: science, ideas and creative activities for all. We will be bringing our virtual reality experience to the festival

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- ❑ **Emerging**: emerging infectious diseases are infections that have recently appeared within a population (e.g. the UK) or those whose which threaten to appear in the near future.
- ❑ **PCR:** a lab test used to detect if a specific organism is present in a sample by testing for its genetic material
- ❑ **Hepatitis**: inflammation of the liver caused by infectious viruses (including hepatitis B virus and hepatitis E virus) and/or non-infectious agents. Hepatitis can lead to a range of health problems, some severe.
- ❑ **Pipeline**: a self-contained series of sequential computing operations to process data
- ❑ **ELISA**: a laboratory technique used to detect and measure specific proteins, antibodies, antigens, or hormones in a sample.
- ❑ **Herpesvirus**: a virus that has DNA as its genetic material and causes herpes infections.
- ❑ **WGS**: Whole genome sequencing is the process of determining the entirety of the DNA sequence of an organism's genome at a single time.
- ❑ **Castanet**: a software pipeline for analysing next generation sequencing data
- ❑ **Screening**: the process of testing a blood sample to detect specific diseases, infections, or other medical conditions
- ❑ **Deferral**: the temporary or permanent postponement of an individual's eligibility to donate blood
- ❑ **Biomarker:** a measurable indicator of a biological state or condition. Biomarkers are often used to diagnose diseases and monitor health condition

BONUS! THREE ADDITIONAL UNMARKED WORDS – can you find them?