CUSTOMER SPOTLIGHT
UNIVERSITY OF ZURICH INSTITUTE OF MEDICAL MICROBIOLOGY

NGS advances bring new opportunities to microbiology research

The MiSeq™ i100 Plus System allows researchers to produce better genomes and address existing challenges with microbial genome sequencing

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The University of Zurich Institute of Medical Microbiology performs basic and clinical microbiology research and provides advanced diagnostic services for the University Hospital Zurich and other hospitals in the region. As part of their mission, the department uses the latest methods to support the best patient care, advanced research, and the education of students.

Next-generation sequencing (NGS) is a core technology for the institute, used to identify and classify microbial species. They recently tested the MiSeq i100 Plus System and MiSeq i100 Series Reagent Kit (1000 cycles) for their microbial genomics applications. We spoke with Dr Helena Seth-Smith, Co-lead of Microbial Genomics Division, about her experience using this setup for her work in NGS diagnostics research and the broader implications for the field of microbiology.

Can you describe your role at the Institute of Medical Microbiology?

Helena Seth-Smith (HS): I am co-lead of the Microbial Genomics Division along with Dr Tim Roloff. I am involved in the analytical side of the department while Dr Roloff is involved in the technical aspects of the department. Between us, we try to cover all the bases. We do bacterial whole-genome sequencing for clinical and research departments within and outside of our institute.

I also run a small research group where we do genome sequencing of bacteria directly from samples that are notoriously difficult to culture.

"We are always working to decrease our turnaround time and decrease our costs. With those things in mind, the MiSeq i100 Plus System works very well for our microbiology applications, and we have built all our bioinformatic pipelines around Illumina data."

What projects are you and your team currently working on?

HS: One of my main research interests is chlamydia. It’s one of my favorite bacteria to work with, but it's also very hard to sequence. You typically have to culture it but, due to modern clinical protocols, most sexually transmitted infection samples go straight into lysis buffer for molecular diagnostics and can't be cultured. However, we are able to isolate genomes from those samples using target enrichment methods.

On another project, we are working with Illumina to expand into respiratory pathogens to study *Mycobacterium tuberculosis*. We are investigating drug resistance and possible transmissions in Swiss clinical isolates.

We are also looking at specific outbreaks in other clinically relevant species, focusing on plasmids, to see where they may have originated.* The study that we're currently doing is on *Enterobacter*, which has large plasmids of around 300 kilobases. These can carry a plethora of resistance determinants. We are investigating where you see the same plasmid appearing in different clones within a species or between different species, how these can occur, and what the implications might be for hospital epidemiology.

What made your lab want to run the MiSeq i100 Plus System over other platforms?

HS: Illumina data is the industry standard for us. We have been customers of Illumina for about ten years, and I have worked with Illumina data since the beginning of NGS. For typing and comparisons of bacteria or reference mapping, Illumina data is the best in our hands. We are always working to decrease our turnaround time and decrease our costs. With those things in mind, the MiSeq i100 Plus System works very well for our microbiology applications, and we have built all our bioinformatic pipelines around Illumina data. It's really the most accurate technology we have found, and the throughput is very good for what we need.

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* Plasmids are circular DNA molecules that are separate from bacterial chromosomes and can be passed between individual bacteria, conferring new genetic material and possibly new functions.

What makes the MiSeq i100 Plus System and MiSeq i100 Series Reagent Kit (1000 cycles) so fitting for infectious disease and microbiology research?

HS: The biggest difference is with read length and the number of contigs that you get out of short-read data. The paired-end data from the MiSeq i100 Plus System with the MiSeq i100 Series 25M Reagent Kit (1000 cycles) offers advantages that can help us identify adjacent regions in the genome or enable more accurate typing of certain species.

What have you been able to do with the MiSeq i100 Plus System that improved the analysis?

HS: We had a very interesting case that was sent to us as a brain biopsy. The team wanted to know if there was a bacterial infection within the brain. Our molecular diagnostic department did 16S ribosomal RNA sequencing, performed using Sanger sequencing, and they didn't find anything. Then, they did internal transcribed spacer (ITS) sequencing for fungal analysis and found a fungal pathogen, although there were a few mismatches, so we wanted to investigate further. We did shotgun metagenomics sequencing on the MiSeq i100 Plus System with the MiSeq i100 Series Reagent Kit (1000 cycles) and blasted the sequence of the ITS region against the CZ ID pipeline for microbiology. We found out it was actually a toxoplasma.

That's the beauty of shotgun metagenomics. You can identify viruses, parasites, bacteria, whatever. It's a hypothesis-free technology and that's why we'd really like to develop that further. And, with the higher data quality, you can get better matches against the databases.

How has access to faster run times and room temperature reagents improved your projects?

HS: Faster run times can lead to faster turnaround times and room temperature reagents reduce the logistic overheads of receiving and storing the reagents. These improvements mean that our pipelines can kick off more rapidly and that we can get the results for downstream analysis faster.

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What future projects are you most excited about?

HS: Personally, I’m excited about the current plasmid work and the genetic context. The MiSeq i100 Plus System and the MiSeq i100 Series Reagent Kit (1000 cycles) have been great for the target enrichment studies that I'm doing with my research group and for generating high-quality data. I think it's just going to give us better genomes.

The MiSeq i100 Plus System and the MiSeq i100 Series Reagent Kit (1000 cycles) have many other potential applications, like characterizing isolates using shotgun metagenomics, where it could have a large impact. I think we will see some interesting advances in microbiome work and 16S ribosomal RNA sequencing, where we could potentially sequence more of the 16S variable regions, providing additional valuable information and better species or lineage identification. It could also help us improve reference genomes that are established but have gaps or support new reference genomes from more clones or more strains.

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