

Case Reports Highlight Role for Sequencing in Detecting Infections Spread by Transplanted Organs

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NEW YORK (GenomeWeb) — According to two recently published case reports, whole genome sequencing can be an important tool in diagnosing infections transmitted to patients through organ transplants, and, if performed more widely in the future, could help physicians better understand the risks posed by transplanting organs from sick donors.

The studies were published online last month in the *American Journal of Transplantation*. One, by a group from the US Centers for Disease Control and Prevention, [reported on](#) using whole-genome sequencing to confirm that two cases of methicillin-resistant *Staphylococcus aureus* infection originated from the same donor. [The other](#), by researchers from the Icahn School of Medicine at Mount Sinai, reported on a single case, also of MRSA infection, which was confirmed using WGS to be the result of transplantation of an infected donor liver.

According to the authors of both case reports, a limited donor pool and expanding transplant waiting lists necessitate the consideration of organs from donors with known bacterial infections. However, there is a lack of hard data on the risks posed by these transplants and the outcomes that can be expected for patients who contract an infection from a transplanted organ.

One reason for this is that only a few cases of suspected organ-borne infections have been analyzed to determine the actual source of infection, and those that have used relatively imprecise techniques, hampering the collection of reliable data on transplant infection rates, associated risk, and patient outcomes.

"Right now there is not enough information to inform truly evidence-based practice guidelines," Andrew Kasarskis, one of the authors of the Mount Sinai group's report, told *Clinical Sequencing News*. "What we don't know is the real risk associated with taking an organ from someone who might be bacterimic and putting into someone else."

According to Kasarskis, previous lower-resolution techniques, which have been applied rarely, lack the ability to undoubtedly confirm transplant infection transmission. "Using a multi-locus typing approach based on PCR markers you're likely to find, for example, that you have a USA300 clone. But that's the troubling clone in every hospital out there, so it tells you nothing about whether it came from the transplant or not."

This was one issue the CDC group discussed in its case study, which analyzed two cases of MRSA in recipients of organs, one liver and one lung transplant, from the same infected donor. Because the strains in all the cases were characterized as USA300, without sequencing there was no way to know whether the

organ recipients had acquired their infections from the donor organs or through some other vector during their hospital stay.

The CDC group used the Illumina MiSeq to compare the genomes of MRSA organisms in two organ recipients and their single donor. Sequencing clearly showed that the donor and recipient MRSA isolates were more closely related to each other than to background strains from other hospital sources.

In the Mount Sinai study, the researchers reported on a single case of post-transplant MRSA in the recipient of a liver from a donor with MRSA mitral valve endocarditis. The group used the PacBio RSII to perform long-read sequencing and then constructed a full de novo assembly of both donor and recipient MRSA isolates, confirming that the two were 100 percent genetically identical.

As in the CDC cases, both the Mount Sinai team's donor and recipient MRSA isolates were USA300 clones. Since nearly all community-acquired MRSA strains in the US originate from USA300, whole genome sequencing and assembly was essential in confirming that the group's case was truly an example of transplant disease transmission, the authors wrote.

"These papers show you can use sequencing to confirm without a shadow of a doubt that an infection came from a donor," Kasarskis said.

According to Kasarskis, increasing the use of sequencing to confirm post-transplant infections will be integral in answering important clinical questions about the safety and utility of organs from infected donors.

For example, in the CDC cases, both infected recipients were treated with antibiotics, but then saw a recurrence of the donor-transmitted MRSA infection much later after being discharged from the hospital, indicating that current standards for post-transplant antibiotic treatment may not be enough to prevent bacterial transmission.

At the same time, another two organ recipients who received kidneys and a pancreas from the same donor had no signs or symptoms of MRSA after transplantation and prophylactic antibiotic treatment.

The two case reports highlight the fact that sequencing has an important role to play in defining cases of true transplant transmission, better understanding complicated patterns of transmission, and advancing clinical strategies to prevent the spread of MRSA and other bacteria through transplant and in other areas of hospital care.



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