Virtual Crossmatch
Newsletter

VIRTUAL CROSSMATCH

What is the goal of histocompatibility testing?

- If recipients have immunological memory against donor antigens, this reduces the chance of a successful transplant outcome.
- Histocompatibility testing aims to detect the presence of donor-specific antibodies (DSA) prior to transplantation – the most well-characterised antibodies are directed against mismatched Human Leucocyte Antigens (HLA).

What are we doing at the moment?

- Patients who are on a transplant waiting list undergo comprehensive testing for HLA antibodies using a Luminex-based assay at least once a year.
- If a strong HLA antibody has been identified, donor offers with this HLA antigen are usually declined.
- A complement-dependent cytotoxicity (CDC) crossmatch test is also performed prior to transplantation as an additional check to exclude the presence of high level DSA.

Why are we changing things?

- The level of detail for donor HLA typing has increased substantially over time, which means that the chance of 'missing' a significant antibody is now very low. As a result, the CDC crossmatch is rarely positive now (and if positive, it is usually a false positive).
- Because the utility of CDC has reduced substantially over time, it is no longer the test of choice in most transplant programmes worldwide. This has resulted in the equipment and reagents for CDC becoming increasingly difficult to source, and we are likely to run out within 12–18 months.

What changes are planned?

- There will be a transition to a virtual crossmatch (VXM) procedure for deceased donor offers. VXM uses detailed information about the HLA antibody profile of recipients combined with accurate HLA typing of the donor to assess whether potentially damaging antibodies are present.

What will VXM look like in practice

Waitlist workup

- Prior to entering the wait list, patients will require full HLA typing and HLA antibody testing as per current practice, noting that this should be limited to patients who have been referred to a transplant unit and authorised for workup.

Waitlist management

- VXM neccessitates an increase in the frequency of antibody screening to reduce the risk of overlooking clinically significant sensitisation.
- It will be vital for clinicians to report potential sensitising events so that additional antibody screening can be performed.
- Clinicians will discuss and list in OrganMatch 'unacceptable antigens'

Organ allocation

- OrganMatch will be able to report on donor HLA type and recipient antigens for exclusion to identify potential organ offer
- Potential recipient lists will be generated in OM as per national organ offer guidelines. Most organ offers will be matched using a VXM, including for: unsensitised recipients, sensitised recipients without a DSA, sensitised recipients with a historic DSA that is not present in current serum, and sensitised recipients with a low risk DSA.

Flow cross match (FXM)

- For certain recipients (for instance where a potential DSA has been identified) the risk of omitting CDC may be increased and therefore a pre-transplant flow crossmatch (FXM) may be undertaken to assist in defining immunological risk based on agreed patient characteristics.
- It will only be feasible to perform a limited number of FXM for a particular deceased donor. The national guidelines will advise on the patient characteristics for conducting a FXM.

- With the transition to VXM, it will be necessary to increase the frequency of HLA antibody screening for patients on transplant waiting lists to minimise the chance of overlooking clinically significant sensitisation (the development of antibodies to potential donors).
- A small proportion of recipients will not be suitable for VXM and will require a physical crossmatch prior to transplantation. In most cases this will be a flow cytometry crossmatch (FXM), which is more sensitive than CDC. However, because only a small number of FXM can be performed for each donor, limited by donor cell numbers and workload, the use of this resource will need to be carefully coordinated to allow equitable access to transplantation for sensitised recipients from all organ groups.
- To facilitate rapid VXM assessment at the time of deceased donor organ offers, the national clinical transplant system (OrganMatch) will be used to manage waiting lists and store information about which HLA antigens should be excluded from transplant offers because of prior sensitisation.
- A set of histocompatibility guidelines will be generated to establish a nationally consistent approach to identifying and managing recipients with HLA antibodies.

When will this happen?

- Transplantation crossmatch processes will change across Australia with the introduction of VXM assessment of histocompatibility from July 2021; current processes for patients on a waiting list will need to be revised from early 2021 in preparation.
- The introduction of FXM instead of CDC is likely to be staged. For abdominal organ offers where a physical crossmatch is needed to confirm histocompatibility, a FXM is likely to become the standard assay from July 2021. FXM will be introduced for thoracic organ recipients after a further 6-12 months to provide more time to make the necessary changes to current practice and to ease pressure on the tissue typing labs.