AST T3 Webinar on the Role of HLA Testing in Pre- and Post-transplant Monitoring for SOT: What it Can and Cannot Tell Us – Additional Q&A

Kathryn Tickam, MD of University Health Network, Toronto

1. With class II B antigens are epitopes of less importance than alpha-beta allele combinations?
Answer: I'm not certain it's an either-or option. Certainly the basis of the immune response is recognition of non-self epitopes.
The issue of alpha beta combinations is that the interaction of the alpha and beta chains creates epitope formations that are not present on the alpha or beta chain in isolation, but only when in a unique combination.
As to importance, the nature of immunogenicity of epitopes, regardless of their chain of origin, is in its infancy of understanding. At this time the epitope "load" is the best metric we have re predicting de novo DSA.

2. How do you obtain donor material for endothelial cross-match?
Answer: The commercially available assay is available through Olerup. It consists of enriching a peripheral cell population with endothelial progenitor cells by magnetic bead separation.
The EPC are then used in a typical FCXM type assay.

3. Is increasing DSA post-tx (kidney, heart, lung) with no evidence of AR an indication to change or intensify immunosuppression? References?
Answer: That is the burning question!!! With the current state of the literature, my personal practice is to not REDUCE immunotherapy (if safe), but there is insufficient evidence to treat on "spec". I do watch these patients with a bit more anxiety and have a low threshold for biopsy. But I think you have precisely identified where large scale well designed trials need to go!

4. Do flow-crossmatch results post-tx correlate with DSA and outcomes?
Answer: As with pre-transplant the flow crossmatch and VXM (DSA) are not perfectly correlated (but are still pretty good and WAY better than when we functioned in a cell based Ab screening era!) for reasons including but not limited to:
1. The FCXM is not a standardized assay and varies widely between labs. Comparing a non standard assay to a non standard assay of course leads to more "noise"
2. The threshold for "calling" Ab varies between labs which will also lead to differences in sensitivity and specificity when comparing to another assay.
3. At the time an Ab is "called" one cannot know what the future donor typing may be. If it happens that a patient ends up with multiple DSA - even if lower "titer" then the FCXM may be positive. If on the other hand they end up with a donor to whom they have only one DSA the FCXM may be negative.
4. Beads may have more antigen density than cells - i.e. more sensitive
5. Ag may conform differently on beans leading to exposure of neoepitopes that are not found in vivo but may lead to non specific and false positive binding
6. Not all ag in the world (there are thousands) can be present on 200 or so beads - (but your lab can always tell you if a particular Ab is not tested for!!) - Though the beads capture most common and a lot of rare - they are not perfect
7. Ab wax and wane over time. if you are looking at a serum from a month ago to do your VXM, but using serum from TODAY in your actual XM - there can be Ab that have appeared or disappeared in that time.
etc etc
The most important thing is to talk to YOUR lab about their correlation and how they see the tests interacting in their hands