4.3. Transmission of HLA alleles from parents to offspring in WGS trios

As additional approach to validate the tool xHLA (18) for calling *HLA* alleles, we assessed whether *HLA* alleles called in offsprings could be traced back to their parents by using WGS data from 75 parent-offspring trios in which the offspring had been diagnosed with SLE (15). Briefly, read mapped to chr6:29000000-34000000 (GRCh37) and unmapped reads were remapped to GRCh38, duplicate reads discarded, and 2-field (i.e. 4-digit) alleles were called for *HLA-A*, *-B*, *-C*, *-DPB1*, *-DQB1* and *-DRB1* using the tool xHLA.

We next evaluated whether the alleles called among the 75 offsprings could be traced back to the parents for each of the 6 *HLA* genes (900 *HLA* alleles in total). The correct transmission pattern was observed for 99.6% of all alleles with 4 wrong allele calls in either the offspring or one of the parents (*HLA-A* for one trio, *-DQB1* for one trio, and *-DPB1* for two trios), therefore showing a high agreement for *HLA* calls.

4.4. Comparison of HLA calls from WGS vs. targeted sequencing data

We next compared 2-field *HLA* calls for overlapping samples with both targeted sequencing data and WGS data (n = 45 SLE patients). For the 6 *HLA* genes, allelic match between calls from targeted sequencing data and WGS data was seen for 95.0% of all genes, and for individual genes, an allelic match of 97.8% (*HLA-A*), 96.7% (*-B*), 84.8% (*-C*), 94.6% (*-DPB1*), 98.8% (*-DQB1*), and 97.8% (*-DRB1*) was seen.

5. C4b deposition on heat-aggregated human IgG

MaxiSorp plates were coated overnight at 4°C with 5 µg/ml heat-aggregated IgG in phosphate buffered saline (PBS) pH 7.4. PBS with 1% bovine serum albumin (BSA) was coated as control. Plates were blocked for 2 hours at room temperature with 1% BSA in PBS. Sera were diluted in GVB++ buffer (2.5 mM veronal buffer [pH 7.3], 150 mM NaCl, 0.1% gelatin, 1 mM $MgCl_2$, 0.15 mM $CaCl_2$) and incubated for 20 min. at room temperature. Deposited C4b was detected with a polyclonal rabbit anti-human C4c antibody (Dako cat. Q0369) followed by HRP-conjugated polyclonal swine anti-rabbit antibody (Dako cat. P0399). Plates were developed using TMB one (Kementec), and absorbance was measured at 450 nm with 620 nm as reference wavelength using a Cytation-5 multi-mode reader (BioTek). Unspecific binding to 1% BSA resulted in $Abs_{450nm-620nm} < 0.02$.

6. Consortia

6.1. The DISSECT consortium

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