Risk-conferring *HLA* variants in an epilepsy cohort: benefits of multifaceted use of whole genome sequencing in clinical practice.

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Purpose: Whole genome sequencing is increasingly used in healthcare, particularly for diagnostics. However, its clinically multifaceted potential for individually-customised diagnostic and therapeutic care remains largely unexploited. We utilised existing whole genome sequencing data to screen for pharmacogenomic risk factors related to antiseizure medication-induced cutaneous adverse drug reactions (cADRs), such as *HLA-B*15:02*, *HLA-A*31:01* variants.

Method: Genotyping results, generated from the Genomics England UK 100,000 Genomes Project primarily for identification of disease-causing variants, were used to additionally screen for relevant *HLA* variants and other pharmacogenomic variants. Medical records were retrospectively reviewed for clinical and cADR phenotypes for *HLA* variant carriers. Descriptive statistics and the chi square test were used to analyse phenotype/genotype data for *HLA* carriers and compare frequencies of additional pharmacogenomic variants between *HLA* carriers with and without cADRs, respectively.

Results: 1043 people with epilepsy were included. Four *HLA-B*15:02* and 86 *HLA-A*31:01* carriers were identified. One out of the four identified *HLA-B*15:02* carriers had suffered antiseizure medication-induced cADRs; the point prevalence of cADRs was 16.9% for *HLA-A*31:01* carriers of European origin (*n*=46) and 14.5% for *HLA-A*31:01* carriers irrespective of ethnicity (*n*=83).

Conclusion: Comprehensive utilisation of genetic data spreads beyond the search for causal variants alone and can be extended to additional clinical benefits such as identifying pharmacogenomic biomarkers which can guide pharmacotherapy for genetically-susceptible individuals.

Keyword 1: Whole genome sequencing

Keyword 2: HLA variants

Keyword 3: Cutaneous adverse drug reactions

Keyword 4: Rash

Keyword 5: Antiseizure medications

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