Consensus statement on adoption of American College of Medical Genetics and Genomics (ACMG) guidelines for sequence variant classification and interpretation

11/11/2016

Headline consensus statement

ACGS recommends adoption of the ACMG guidelines (Richards, 2015) for sequence variant classification and interpretation in UK diagnostic genetic laboratories carrying out testing for rare disease and familial cancers.

Background

Classification and interpretation of genomic variation is a highly complex discipline and in the clinical setting the need for accuracy and consistency is essential to maximise patient benefit and minimise harm. The revolution in genomic technology has led to increased routine detection of novel variants in a rapidly increasing number of novel disease genes. ACMG recently attempted to address the challenges faced by devising a detailed systematic framework for sequence variant interpretation which has now been widely adopted in the US and many European centres. Furthermore, expert panels are being formed as part of the ClinGen resource consortium to develop gene and disease specific criteria to supplement the original framework.

A Workshop hosted by ACGS was held at Austin Court, Birmingham on 4th November 2016 to reach an expert consensus view on adoption of the ACMG guidelines by the UK clinical genomics community. 70 delegates attended representing most Regional Genetics services (lab and clinical teams) with additional invited representation from all BSGM constituent groups, NHS-E (Genomics Implementation Unit), Genomics England, UKNEQAS, UKGTN, DECIPHER/DDD, HEE (Genomics Education Programme) and PHG-Foundation. The agenda included presentations on NEQAS assessment of consistency in interpretation, experiences in early adoption of ACMG guidelines, harmonisation with CNV classification, frameworks for clinical/phenotypic classification, and integration of ACMG framework into DECIPHER, together with breakout group discussions. A summary report of the Workshop is being prepared by PHG-Foundation for circulation in early 2017.

There was clear consensus agreement that the UK clinical genomics community should adopt ACMG sequence interpretation guidelines as soon as possible. ACGS, with support from HEE, will develop a multi-disciplinary training approach starting with a train-the-trainer event in early 2017. This will catalyse centre and region based adoption and also identify UK specific issues which may augment the guidelines when they are built into UK Best Practice guidelines. ACGS and BSGM annual meetings in 2017 will incorporate updates on progress with these important initiatives. In addition ACGS will offer to support further guideline development with ClinGen and ACMG via distributed variant data analyses.

Signed by: **Dom McMullan | Chair, ACGS**

Endorsed by: **Professor Bill Newman | Chair, BSGM**