TGLclinical

TGLclinical use the **CIGMA** system to assess variants detected.

CIGMA (Clinical Impact of Genetic Mutation Analysis) is a variant classification system developed at the Institute of Cancer Research by Clinician-Scientists, combining expertise in the genetic cancer predisposition, clinical genetics, molecular genetics, genetic epidemiology, data-mining and large-scale bioinformatics.

The **CIGMA** system is based on expert curation of relevant resources, bioinformatic integration of these inputs and detailed per-variant literature review followed by application of a classification algorithm.

The **CIGMA** classification algorithm uses gene-level inputs, including biological and genetic parameters and variant-level inputs, including but not limited to data from multiple sources of exome/genome sequences, locus-specific databases, genetic epidemiologic multi-factorial analyses, in-silico prediction tools and validated functional assays.

The output classification structures are defined per gene and by phenotype. The individual output classifications comprise a numeric value and a letter. The numeric value corresponds to the clinical management class and the letter corresponds to the strength of evidence.

For example, the output classifications for variants detected in BRCA1/BRCA2 in testing for autosomal dominant predisposition to hereditary breast-ovarian cancer are:

<u>Class1: Manage as pathogenic</u>

1A: pathogenic

1B: highly likely pathogenic

<u>Class 2: Manage as non-pathogenic</u>

2A: not pathogenic

2B: unlikely pathogenic

2C: unclear information currently available, ongoing review recommended