CIMRA

Diagnostic tools to assess pathogenicity of MMR genes variants.

The CIMRA assay is developed, calibrated and validated by the DNA replication and responses to DNA damage group (PI: dr. De Wind) of the department of Human Genetics (LUMC, Leiden). The CIMRA assay is an *in vitro* assay to classify VUS in the four MMR genes, identified in individuals suspected of Lynch syndrome [1-3]. This assay is endorsed as diagnostic test by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Expert Panel and is used to classify MMR gene variants in the Dutch population, in the framework of the nation-wide INVUSE consortium. The CIMRA assay is currently implemented in the diagnostic routine of the Department of Clinical Genetics and is offered worldwide. CIMRA is suitable for testing missense variants but not intronic, synonymous, splice, or large insertion/deletion variants. It can be used as supporting evidence for the PS3/BS3 criteria in ClinGen variant classification (https://cspec.genome.network/cspec/ui/svi/). CIMRA is a cell-free in vitro MMR activity test. No patient material is required for this test. The turnaround time is 20–22 weeks, and the cost is €2,727 per variant tested. CIMRA can be requested here.

[1] Drost, M. et al. A functional assay-based procedure to classify mismatch repair gene variants in Lynch syndrome. Genet Med 21, 1486-1496 (2019).

[2] Drost, M. et al. Two integrated and highly predictive functional analysis-based procedures for the classification of MSH6 variants in Lynch syndrome. Genet Med 22, 847-856 (2020).

[3] Rayner, E. et al. Predictive functional assay-based classification of PMS2 variants in Lynch syndrome. Hum Mutat 43, 1249-1258 (2022).

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