ESTABLISHED INNOVATIONS IN DIAGNOSTICS

Confirmatory testing for Congenital Adrenal Hyperplasia (CAH)

Detect *CYP21A2* variants - including deletions and duplications - in a fast and cost-efficient way

CAH and confirmatory testing

Congenital adrenal hyperplasia (CAH) summarizes metabolic disorders that lead to inadequate synthesis of adrenal steroid hormones (cortisol, aldosterone). By far the most frequent form of CAH is caused by genetic variants in the *CYP21A2* gene encoding for steroid 21-hydroxylase.

The clinical presentation is highly variable and includes virilization of female newborns and life-threatening salt-wasting conditions.[1] Since early treatment is desirable, CAH newborn screening programs based on 17-hydroxyprogesteron (17-OHP) levels have been introduced in many countries. However, due to the high false-positive rate of 17-OHP assays, a second-tier test using liquid chromatography-tandem mass spectroscopy or molecular genetic analysis may be necessary.[2]

ViennaLab has developed two complementary genotyping assays for early and reliable confirmation of CAH:

The combination of **CAH StripAssay®** and **CAH RealFast™ CNV Assay** pinpoints the most frequent *CYP21A2* variants including deletions and duplications.

Key features of ViennaLab CAH Assays

- Comprehensive reporting by using both assays
- CAH StripAssay® for detection of *CYP21A2* single nucleotide variants
- CAH RealFast™ CNV Assay for *CYP21A2* deletions and duplications
- Cost-efficient technology
- Fast and easy workflow

CE IVD

Order information: • CAH StripAssay®: 4-380/4-380-A (20/48 tests) • CAH RealFast™ CNV Assay: 7-410 (100 reactions)

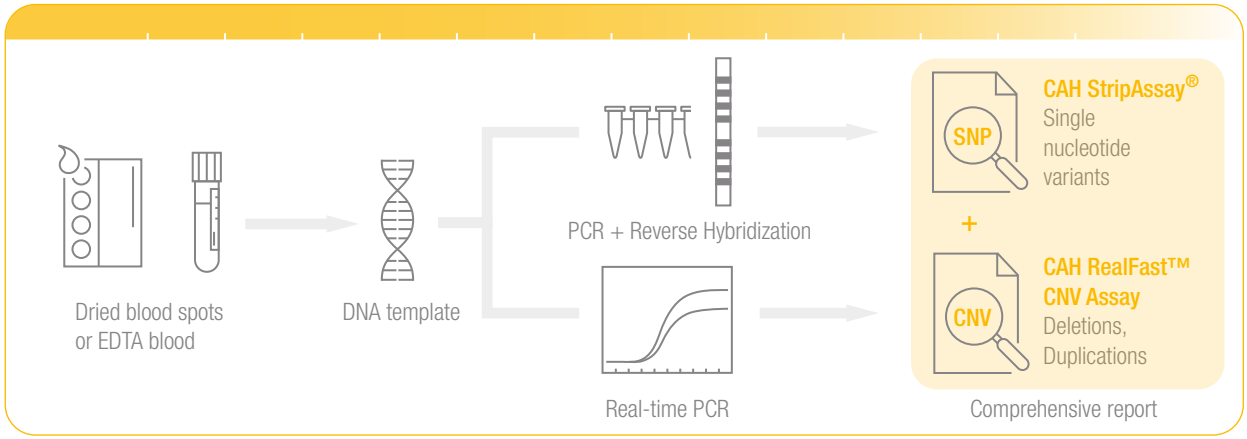
CYP21A2 variants covered by ViennaLab CAH Assays

The CAH StripAssay® covers the 11 most prevalent single nucleotide variants and a small deletion in the *CYP21A2* gene. Twenty to 25% of pathogenic variants are large *CYP21A2* deletions, duplications or chimeric genes.[3] Therefore, assessment of the *CYP21A2* copy number variation (CNV) is crucial for diagnosis. The combination of both, CAH StripAssay® and CAH RealFast™ CNV Assay is a faster and more cost-efficient targeted analysis compared to sequencing the whole gene and CNV analysis by MLPA.[4] In total, ViennaLab CAH assays have a detection rate of up to 94%.[5]

CAH Assays	*CYP21A2* variants											
	Copy Number Variation	P30L [P31L]	I2 splice	Del 8 bp E3	I172N [I173N]	Cluster E6	V281L [V282L]	L307fs [L308fs]	Q318X [Q319X]	R356W [R357W]	P453S [P454S]	R483P [R484P]
StripAssay®		x	x	x	x	x	x	x	x	x	x	x
RealFast™	x											

The *CYP21A2* gene may harbour polymorphisms affecting the numbering of codons, thus differences in nomenclature exist in literature. Predicted protein changes referring to NP_000491.4 are in parenthesis.

Workflow of ViennaLab CAH Assays



Workflow of ViennaLab CAH assays. Generate a ready-to-use PCR template from blood or dried blood spots (e.g. by using GEN^{X}TRACT™ Blood DNA Extraction System). Run the CAH StripAssay® and CAH RealFast™ CNV Assay simultaneously according to the instructions for use and combine the results to a single comprehensive report at the end.

References:

1. Speiser PW, White PC. Congenital adrenal hyperplasia. N Engl J Med. 2003;349:776-88.

2. White PC. Update on diagnosis and management of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Curr Opin Endocrinol Diabetes Obes. 2018 Jun;25(3):178-184.

3. Concolino P, Costella A. Congenital Adrenal Hyperplasia (CAH) due to 21-Hydroxylase Deficiency: A Comprehensive Focus on 233 Pathogenic Variants of *CYP21A2* Gene. Mol Diagn Ther. 2018;22:261-280.

4. Baumgartner-Parzer S, Witsch-Baumgartner M, Hoeppner W. EMQN best practice guidelines for molecular genetic testing and reporting of 21-hydroxylase deficiency. Eur J Hum Genet. 2020 Oct;28(10):1341-1367.

5. Németh S, Riedl S et al. Reverse-hybridization assay for rapid detection of common *CYP21A2* mutations in dried blood spots from newborns with elevated 17-OH progesterone. Clin Chim Acta. 2012;414:211-4.

Manufacturer:
ViennaLab Diagnostics GmbH
Gaudenzdorfer Guertel 43-45
A-1120 Vienna, Austria
www.viennalab.com
t: (+43-1) 8120156-0
e: info@viennalab.com

Distributor:

October 2022 • ISO 13485

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