

Congenital Stationary Night Blindness test

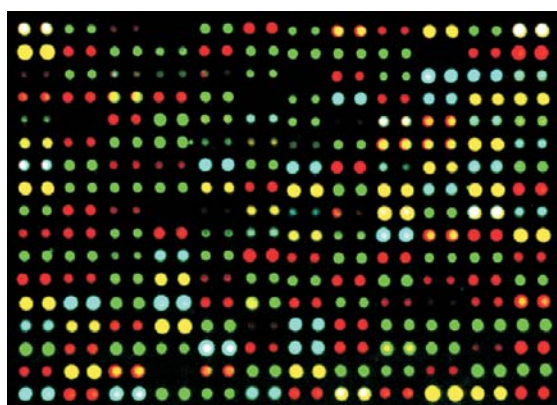
ABOUT ASPER OPTHALMICS

Asper Ophthalmics is a division of Asper Biotech. Together with our partners, Asper has developed a portfolio of ophthalmogenetic DNA tests. This list continues to expand in coming years. Since ophthalmogenetics has become a major part of our efforts, and we see increasing potential in the future, Asper Ophthalmics was established. Asper Ophthalmics combines the experience and reputation of renowned partners and high quality DNA testing of Asper Biotech. We wish to be the partner of choice for all those involved in ophthalmogenetics research institutions, DNA testing centers, patient organisations, and commercial entities.

THE CHIP

Congenital stationary night blindness (CSNB) consists of a group of eye disorders clinically characterized by a non-progressive severe deficiency of vision under dim illumination. The genetic test has been developed for screening mutations of three forms of CSNB: autosomal dominant (ad), autosomal recessive (ar) and X-linked (xl) CSNB. Currently the test can be used for screening of 126 mutations in 9 genes: RHO, PDE6B, GNAT1, CABP4, GRM6, SAG, NYX, CACNA1F and CACNA2D.

Development and chip validation experiments have been performed in collaboration with Dr. Christina Zeitz and Prof. Dr. Wolfgang Berger, Division of Medical Molecular Genetics and Gene Diagnostics, Institute of Medical Genetics of the Univeristy of Zurich.

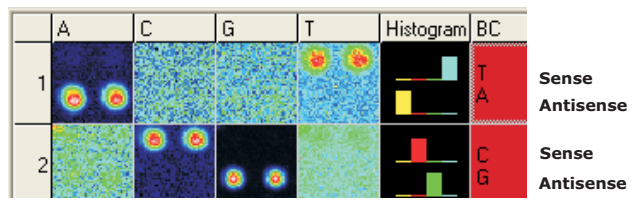


Fragment of CSNB chip for simultaneous screening of 126 mutations. The image above shows pseudocolor signals (A-yellow, C-red, G-green, T-cyan).

APEX

Arrayed Primer EXtension is a genotyping technology that combines the efficiency of a microarray-based assay with the comparable accuracy of the Sanger dideoxy sequencing.

For further information please contact Asper Biotech info@asperbio.com.



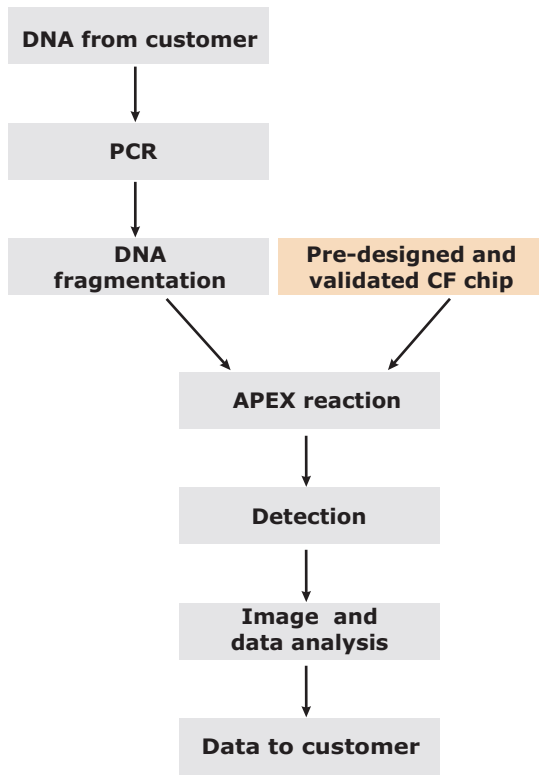
Wild type and homozygous nucleotide change T>C in position 1214 of GRM6 gene analyzed by APEX. The signals corresponding to C in the sense strand and G in the antisense strand are indicative for mutation. The mutation causes amino acid change I405T.

THE PROCESS

Genomic DNA samples will be sent to Asper. Amplification reaction will be performed by using PCR, followed by fragmentation and purification reactions. Microarray slides will be prepared and quality controlled. APEX reaction will be performed and scanned followed by analysis of images. After careful analysis of the images some mutations will be sent for re-analysis. Report will be established and sent out to the partner. Follow-up support will be provided if necessary to explain the results.

In addition, to confirm the results with secondary method, Asper provides verification of the APEX findings by dideoxy sequencing on Applied Biosystems 3130 Genetic Analyzer.

ROUTINE SCREENING OF DNA SAMPLES



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REQUIREMENTS FOR THE DNA SAMPLES

- The quality of the DNA needs to be ensured by our partner.
- 2,5 µg of genomic DNA is required for CSNB chip analysis.
- Preferred concentration range is 100-250 ng/µl.
- DNA samples to be solved in pure sterile water.

TURNAROUND TIME

Express delivery – The results will be delivered in 3 – 5 working days after the arrival of samples.

Standard delivery – The results will be delivered approximately in 3 – 6 weeks after the arrival of samples.

OTHER TESTS PROVIDED BY ASPER

Asper Biotech	Asper Ophthalmics
Thalassemia	Stargardt disease
Cystic Fibrosis	Leber's congenital amaurosis
DNA repair	Usher syndrome
Hereditary Hearing Loss	Aut. Rec. Retinitis Pigmentosa
Ashkenazi Jewish	Aut. Dom. Retinitis pigmentosa
	Bardet Biedl syndrome
	Aut. Dom. Optic Atrophy
	Con. Stat. Night Blindness
	Corneal Dystrophy

RECOMMENDATIONS FOR SHIPMENT OF THE SAMPLES

- For speedy and secure delivery, international courier services, for example DHL, UPS and FedEx, are recommended; alternatively, you can send samples by air mail as a small parcel.
- Since high quality DNA samples are stable, there is no need for shipment in dry or wet ice.
- Care should be taken to avoid drying out; please use either screw cap tubes or wrap the caps of each Eppendorf tube with parafilm.
- In order to avoid damage to the tubes during shipment, a tube storage box made of plastic or cardboard, and doubling it with a padded envelope, is recommended. Please avoid using round containers, such as 50 ml Corning tubes, for tube protection.
- Send samples to the following address:
Asper Biotech
Oru 3
Tartu 51014
Estonia
Ph: +372 7 441 556
- Please fill in the DNA sample submission form (download the file from webpage) which improves and accelerates the handling of DNA samples and include it in the package.
- Notify us by email (Info@asperbio.com, or the respective project manager), including the number of samples, which test is to be performed and tracking data).
- Enclose in the package the list of samples, which test is to be performed and quality data, if available.
- Please make sure that the declared value for the package in the shipment documents does not exceed 10 EUR (USD).

FOR FURTHER INFORMATION

1. **Molecular genetics and protein function involved in nocturnal vision.**
Zeit C. 2007. Expert Review of Ophthalmology 2:467-48
2. **Mutation in the Auxiliary Calcium-Channel Subunit CACNA2D4 Causes Autosomal Recessive Cone Dystrophy.**
Wycisk K, Zeitz C, Feil S, Wittmer M, Forster U, Neidhardt J, Wissinger B, Zrenner E, Wilke R, Kohl S, Berger W. 2006. Am J Hum Genet 79:973-977.
3. **Mutations in CABP4, the Gene Encoding the Ca²⁺-Binding Protein 4, Cause Autosomal Recessive Night Blindness.**
Zeit C, Kloeckener-Gruissem B, Forster U, Kohl S, Magyar I, Wissinger B, Matyas G, Borruat FX, Schorderet DF, Zrenner E, Munier FL, Berger W. 2006. Am J Hum Genet 79:657-667.
4. **Mutations in GRM6 cause autosomal recessive congenital stationary night blindness with a distinctive scotopic 15 Hz flicker electroretinogram (ERG).**
Zeit C, van Genderen M, Neidhardt J, Luhmann UFO, Hoeben F, Forster U, Wycisk K, Mátyás G, Hoyng CB, Riemsdag F, Meire F, Cremers FPM, Berger W. 2005. Invest Ophthalmol 46:4328-4335.
5. **Night blindness and abnormal cone electroretinogram ON responses in patients with mutations in the GRM6 gene encoding mGluR6.**
Dryja TP, McGee TL, Berson EL, Fishman GA, Sandberg MA, Alexander KR, Derlacki DJ, Rajagopalan AS. 2005. Proc Natl Acad Sci U S A 102:4884-4889.
6. **The complete form of X-linked congenital stationary night blindness is caused by mutations in a gene encoding a leucine-rich repeat protein.**
Pusch CM, Zeitz C, Brandau O, Pesch K, Achatz H, Feil S, Scharfe C, Maurer J, Jacobi FK, Pinckers A, Andreasson S, Hardcastle A, Wissinger B, Berger W, Meindl A. 2000. Nat Genet 26:324-327.
7. **An L-type calcium-channel gene mutated in incomplete X-linked congenital stationary night blindness.**
Strom TM, Nyakatura G, Apfelstedt-Sylla E, Hellebrand H, Lorenz B, Weber BH, Wutz K, Gutwillinger N, Ruther K, Drescher B, Sauer C, Zrenner E, Meitinger T, Rosenthal A, Meindl A. 1998. Nat Genet 19:260-263.
8. **Loss-of-function mutations in a calcium-channel alpha1-subunit gene in Xp11.23 cause incomplete X-linked congenital stationary night blindness.**
Bech-Hansen NT, Naylor MJ, Maybaum TA, Pearce WG, Koop B, Fishman GA, Mets M, Musarella MA, Boycott KM. 1998. Nat Genet 19:264-267.