ABCR genetic testing

Stargardt disease, cone-rod dystrophy

ASPER OPHTHALMICS
www.asperophthalmics.com

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Asper Ophthalmics is a division of Asper Biotech. Asper Biotech has developed a number of DNA testing applications during its operations, and since the scope of the business has been growing, we feel we need to focus on the most important areas of our business.

Together with our partners, Asper has developed a portfolio of ophthalmic DNA tests. This list continues to expand in coming years. Since ophthalmics has become a major part of our operations, and we see increasing potential in the future, Asper Ophthalmics was created.

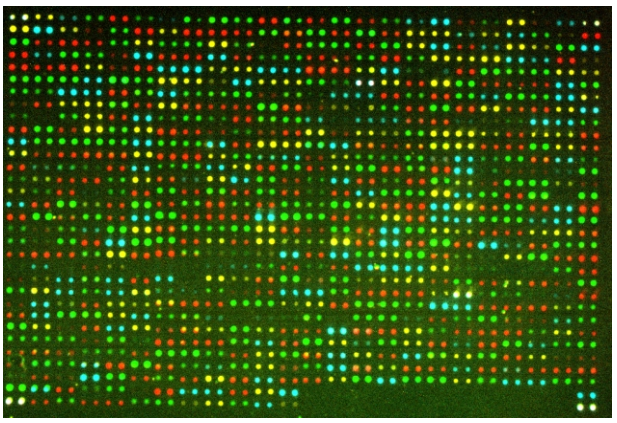
Asper Ophthalmics combines the experience and reputation of good partner and high quality DNA testing company of Asper Biotech, as well as our increasing focus on ophthalmics. We wish to be the partner of choice for all those involved in ophthalmics genetics – research institutions, DNA testing centers, patient organizations, commercial entities.

THE CHIP

Genetic variations in the ABCR gene have been associated with several retinal phenotypes, including Stargardt disease/fundus flavimaculatus, cone rode dystrophy. Genetic analyses of ABCR variations have been complicated by substantial allelic heterogeneity and by differences in screening methods. To overcome these limitations, a APEX genotyping microarray (chip) was designed for looking known variations in ABCR gene.

The current version of ABCR gene chip consists of 519 mutations and will be updated once new mutations will become available. Comparative tests have been made by using direct sequencing, SSCP technologies and APEX based ABCR test was able to test more than 98% of the existing genetic variations.

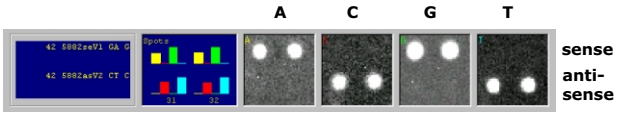
Thousands of DNA samples have been analyzed by using the ABCR gene chip. Our partners have been Columbia University, Baylor College of Medicine, University Medical Center Njimegen and many others.



ABCR gene mutation detection chip for simultaneous screening of 519 mutations. The image above shows pseudocolor signals (A-yellow, C-red, G-green, T-cyan).

APEX

Arrayed **P**rimer **EX**tension is a genotyping technology that combines the efficiency of a microarray-based assay with the comparable accuracy of the Sanger dideoxy sequencing.



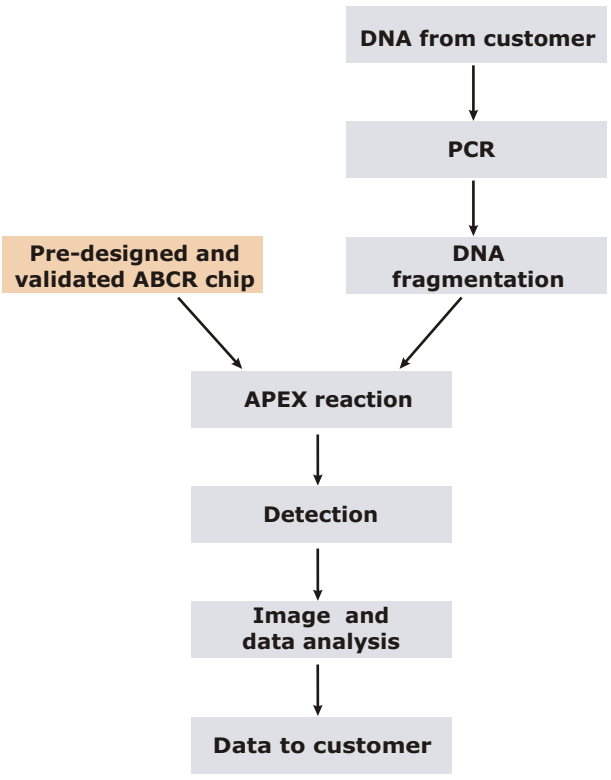
Nucleotide change G>A in position 5882 of ABCR gene exon 42 analyzed by APEX. The signals corresponding to A in the sense strand and T in the antisense strand are indicative for mutation. The mutation causes amino acid change G1961E.

THE PROCESS

DNA sample analysis will be performed under ISO:9001:2000 quality control regulations. 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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Stargardt disease, cone-rod dystrophy, age related macular degeneration

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REQUIREMENTS FOR THE DNA SAMPLES

- **The DNA quality needs to be ensured.**
- **3 µg of genomic DNA is required for ABCR chip analysis.**
- **Preferred concentration range of DNA is 100-250 ng/µl.**
- **DNA samples should be provided 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
Wilson disease	Bardet Biedl syndrome
Breast and Ovarian canc.	Aut. Dom. Optic Atrophy
	Con. Stat. Night Blindness
	Corneal Dystrophy
	Vitelliform Macular 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
  Vaksali 17a
  Tartu 50410
  Estonia
  Ph: +372 7307 295
- **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@asperophthalmics.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. **Microarray-based mutation analysis of the ABCA4 gene in Spanish patients with Stargardt disease: evidence of a prevalent mutated allele**
   Diana Valverde, R. Riveiro-Alvarez, Sara Bernal, Kaie Jaakson, Montserrat Baiget, Rafael Navarro, Carmen Ayuso Molecular Vision 2006; 12:902-908
2. **Microarray-based mutation analysis of the ABCA4 (ABCR) gene in autosomal recessive cone-rod dystrophy and retinitis pigmentosa.**
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   European Journal of Human Genetics (2004) 12, 1024–1032.
3. **Genotyping Microarray (Gene Chip) for the ABCR (ABCA4) Gene**
   K. Jaakson, J. Zernant, M. Kulm, A. Hutchinson, N. Tonisson, D. Glavaci, M. Ravnik-Glavaci, M. Hawlina, M.R. Meltzer, R.C. Caruso, F. Testa, A. Maugeri, C.B. Hoyng, P. Gouras, F. Simonelli, R.A. Lewis, J.R. Lupski, F.P.M. Cremers, and R. Allikmets
   Hum Mutat 2003, Vol. 22, pp. 395–403.
4. **Genotyping microarray (disease chip) for leber congenital amaurosis: detection of modifier alleles.**
   Zernant J, Kulm M, Dharmaraj S, den Hollander AI, Perrault I, Preising MN, Lorenz B, Kaplan J, Cremers FP, Maumenee I, Koenekoop RK, Allikmets R.
   Invest Ophthalmol Vis Sci. 2005 Sep;46(9):3052-9.
5. **Genotyping Microarray for the Detection of More Than 200 CFTR Mutations in Ethnically Diverse Populations.**
   Schrijver I, Oitmaa E, Metspalu A, Gardner P.
   J Mol Diagn. 2005 Aug;7(3):375-87
6. **A first-generation linkage disequilibrium map of human chromosome 22.**
   Dawson, E., Abecasis, G.R, Bumpstead, S., Chen, Y., Hunt, S., Beare, D.M., Pabial, J., Dibling, T., Tinsley, E., Kirby, S., Carter, D., Papaspyridonos, M., Livingstone, S., Ganske, R., Lõhmussaar, E., Zernant, J., Tõnisson, N., Remm, M., Mägi, R., Puurand, T., Vilo, V., Kurg, A., Rice, K., Deloukas, P., Mott, R., Metspalu, A., Bentley, D. R., Cardon, L.R. and Dunham, I.
   Nature, August 2002, Vol. 418, pp. 544-548.

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