Get to know a gene: ANK3

Summary: ANK3 has not been shown to inform on patient medication response and therefore is not a pharmacogenomic marker. As a disease marker, it lacks clinical utility. There is an association between ANK3 and bipolar disorder, but the contribution of ANK3 to disease risk is very small. Therefore, genetic testing for ANK3 is not recommended at this time.

What is ANK3?

ANK3 encodes Ankyrin-G, a protein that is important for the function of sodium ion channels and modulation of neuronal excitability. While ANK3 has been studied as a potential disease marker for bipolar disorder and schizophrenia, there are currently no studies investigating the effect of ANK3 variants on response to psychiatric medications.

Is ANK3 a risk factor for bipolar disorder and schizophrenia disease states?

Single nucleotide polymorphisms (SNPs) within ANK3 have consistently reached genome-wide significance ($p<5 \times 10^{-8}$) for an association with bipolar disorder.[1–3] However, the effect size is small (OR=1.27-1.45), and ANK3 is only one of many susceptibility genes that impact the risk for bipolar disorder. Some of the many other genes associated with bipolar disorder include CACNA1C, TRANK1, and MHC.[2,4] SNPs within ANK3 failed to reach genome-wide significance for an association with schizophrenia.[5–7]

What is the clinical significance of ANK3 genotyping?

Although ANK3 may be involved in the biology of disease, it is not useful for predicting how a patient will respond to medications. There are currently no studies investigating the effect of ANK3 variants on psychiatric treatment response. Therefore, ANK3 is not a pharmacogenomic marker and is not currently included on the GeneSight® test panels.

While a positive association has been shown between ANK3 and bipolar disorder[1–3], an association between ANK3 and schizophrenia has not been supported[5–7]. It has been hypothesized that a potential reason ANK3 may play a role in bipolar disorder is that variation in ANK3 may result in dysregulation of sodium ion channels, which may increase excitatory signaling in the brain and affect mood regulation. However, while ANK3 is valid as a marker for bipolar disorder, the actual contribution of ANK3 to disease risk is very small, and ANK3 is only one of many susceptibility genes. Without a proper understanding of the modest clinical impact of ANK3 variation, testing for ANK3 may lead to overestimation of disease risk, unnecessary use of antipsychotic and mood stabilizing medications, and undue patient anxiety regarding the development of serious conditions. Therefore, genetic testing for ANK3 is not recommended at this time.

For more information, contact the Assurex Health Medical Information Department at:

PHONE: 855.891.9415

EMAIL: medinfo@assurexhealth.com

genesight®

References

1. Ferreira, M., O'Donovan, M. & Meng, Y. Collaborative genome-wide association analysis supports a role for ANK3 and CACNA1C in bipolar disorder. Nat. ... 40, 1056–1058 (2008).
2. Chen, D. T. et al. Genome-wide association study meta-analysis of European and Asian-ancestry samples identifies three novel loci associated with bipolar disorder. Mol. Psychiatry 18, 195–205 (2013).
3. Mühleisen, T. W. et al. Genome-wide association study reveals two new risk loci for bipolar disorder. Nat. Commun. 5, 3339 (2014).
4. Ruderfer, D. M. et al. Polygenic dissection of diagnosis and clinical dimensions of bipolar disorder and schizophrenia. Mol Psychiatry 19, 1017–1024 (2014).
5. Athanasiu, L., Mattingsdal, M. & Kähler, A. Gene variants associated with schizophrenia in a Norwegian genome-wide study are replicated in a large European cohort. J. Psychiatr. ... 44, 748–753 (2010).
6. Ripke, S., Sanders, A. & Kendler, K. Genome-wide association study identifies five new schizophrenia loci. Nat. ... 43, 969–976 (2011).
7. Bergen, S. E. et al. Genome-wide association in a Swedish population yields support for greater CNV and MHC involvement in schizophrenia compared with bipolar disorder. Mol Psychiatry 17, 880–886 (2012

Assurex HEALTH