

Pharmacogenetic Panel and Algorithm for Predicting Antipsychotic-Induced Weight Gain

Market Need

While antipsychotic treatment leads to successful remission for some schizophrenia patients, there is large inter-individual variability both in treatment efficacy and adverse effects, amongst which a major life-threatening consequence is antipsychotic induced weight gain (AIWG) and its related complications. The prevalence of schizophrenia is ~1% of the general population. Around 30% of patients develop weight gain following initial treatment with 2nd generation antipsychotics, and 30-40% overall go on to develop metabolic syndrome. Pharmacogenetic-based algorithms have a high potential to identify individuals who are at risk for development of AIWG. These, in turn, can greatly aid in the decision making process for antipsychotic treatment.

Technology Description

The present technology is a pharmacogenetic panel which makes use of polymorphisms in the genes modulating the appetite and satiety pathways (e.g. Neuropeptide Y, Melanocortin 4 receptor, Orexin receptor 2, Glucagon, Cannabinoid receptor among others), coupled with an algorithm to predict the likelihood of weight gain following treatment with antipsychotic drugs such as clozapine and olanzapine. The algorithm classifies patients into high risk (likelihood of over 7% weight gain), moderate risk (2 to 7% weight gain) and low risk (less than 2% weight gain). The test is administered prior to treatment. A high risk individual would then be advised to not use AIWG-related drugs, or use them with caution and more intensive monitoring.

Stage of Development

- The technology was initially tested on a subset of a sample 218 schizophrenia or schizoaffective disorder patients.
- Currently undergoing clinical validation as part of a randomized controlled trial.

Advantages

- A priori detection and quantification of the risk of AIWG before antipsychotic treatment
- Facilitates the correct selection of medication and/or dosage regimes not likely to cause AIWG
- Saves healthcare payer funds by de-escalating co-morbidities of antipsychotic-treated illnesses

Notable Publication(s)

- Tiwari AK, et al. (2016). Association of orexin receptor polymorphisms with antipsychotic-induced weight gain. *World J Biol Psych* 17: 221-229.
- Zai CC, et al. (2015). Association study of GABAA alpha2receptor subunit gene variants in antipsychotic-associated weight gain. *J Clin Psychopharmacol* 35: 7-12.
- Pouget JG, et al. (2015). Investigation of TSPO variants in schizophrenia and antipsychotic treatment outcomes. *Pharmacogenomics* 16: 5-22.
- Brandl EJ, et al. (2014). Genetic variation in GCG and in the GLP1R genes and antipsychotic-induced weight gain. *Pharmacogenomics* 15: 423-431.
- Goncalves VF, et al. (2014). A hypothesis-driven association study of 28 nuclear-encoded mitochondrial genes with antipsychotic-induced weight gain in schizophrenia. *Neuropsychopharmacology* 39: 1347-1354. www.sciencedirect.com/science/article/pii/S1056871916301708

Intellectual Property

The multigene AIWG panel is protected by a nationalized PCT (publication WO2015127557) with applications pending in CA and granted in US (10,662,475), AU, JP, IL.

The GABRA1 polymorphisms and uses are protected by a nationalized PCT (publication WO2015054792) with patents issued in US (10,301,678), CA, JP, IL, AU, KR.

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