Genetic test shows risk for serious adverse reaction to toxic goitre treatment

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Researchers and doctors at Uppsala University, along with Swedish and international collaboration partners, have found gene variants that predict the risk of a serious adverse reaction to drugs used for the treatment of hyperthyroidism. The results are published in *The Lancet Diabetes & Endocrinology*.

Adverse drugs reactions are a leading cause of admission to hospital. Genetic variation is believed to contribute to a majority of serious immune-mediated adverse drug reactions. These reactions are being studied by the Swedegene project led by Pär Hallberg and Mia Wadelius at the Department of Medical Sciences, Clinical Pharmacology at Uppsala University, in collaboration with the Swedish Medical Products Agency, Karolinska Institutet and a large number of international researchers and doctors. The aim is to develop tests to predict patients at high risk of suffering side-effects so that they can be offered other treatment. In the long run, this could lead to safer and more individualised treatment.

'Our long-term work has now started to yield results. We systematically collect samples from patients with serious side-effects in Sweden and we work in collaboration with other countries. Thanks to the participation of patients in Sweden, Spain, France and Germany, we can now predict the risk of suffering a serious side-effect of medication against toxic goitre,' says Pär Hallberg, chief physician and associate professor at Clinical Chemistry and Pharmacology, Uppsala University Hospital (Akademiska sjukhuset) who also set up the European Drug Induced Agranulocytosis

Consortium (EUDAC).

'Some patients treated with medication for hyperthyroidism, such as thiamazole (methimazole), carbimazole or propylthiouracil, react with agranulocytosis which is a lack of white blood cells that suppresses the immune system. We've shown that certain immune genes increase the risk of agranulocytosis 750 times in Europeans. This gives us an opportunity to individualise treatment using genetic testing and thus avoid an unnecessary adverse reaction,' says Mia Wadelius, senior physician and lecturer at Clinical Chemistry and Pharmacology, Uppsala University Hospital who is the lead author of the article.

'These discoveries confirm the value of working with Swedegene which began in 2008. We have the infrastructure and the ambition to bring in many more patients who suffer from other side-effects. In addition to our present article, we already have a number of promising results that will be published,' says Pär Hallberg.

More information: Hallberg P, Eriksson N, Ibañez L, Bondon-Guitton E, Kreutz R, Carvajal A, Lucena M, Sancho Ponce E, Sainz Gill M, Douros A, Lapeyre-Mestre M, Montastruc JL, Ruiz-Nuñes J, Stephens CM, Martin J, Axelsson T, Yue QY, Magnusson PK, Wadelius M, on behalf of EuDAC. Genetic variants associated with antithyroid drug-induced agranulocytosis: a genome-wide association study in a European population. *Lancet Diabetes Endocrinol*. Epub 2016 May 3 2016.

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