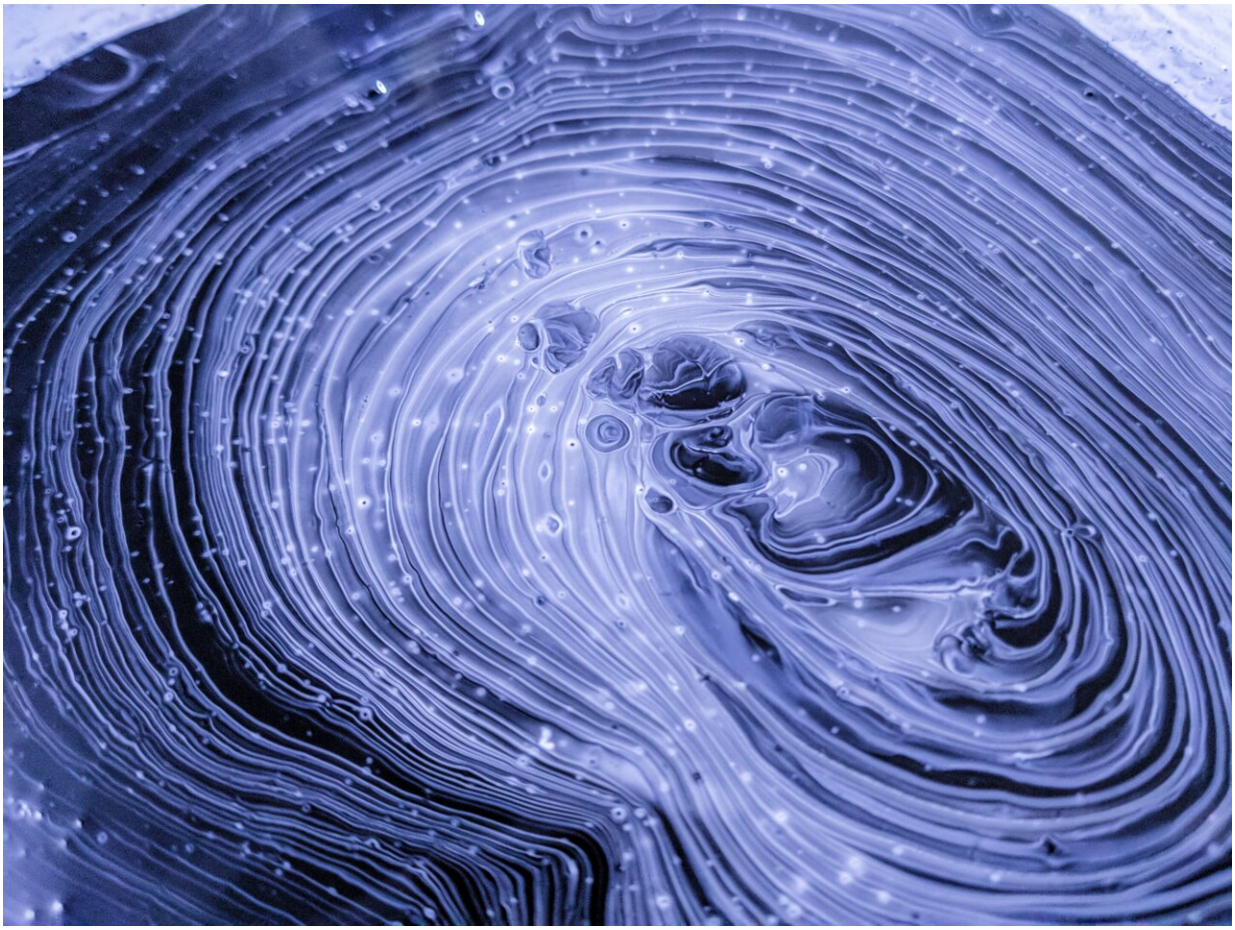
MedicalXpress

Scientists localise genetic mutations responsible for abnormal thyroid function

January 16 2013, by Kerry Faulkner



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Thyroid hormone resistance has been linked to mutations in the IGSF1

gene for the first time—surprising researchers who did not suspect it played a role in the maintenance of normal thyroid function.

The thyroid hormone regulates metabolism and plays an important role in development. Deficiencies, especially during intrauterine life and immediately post-natal, can result in damage of the central nervous system.

Co-author and Winthrop Professor Timothy Davis from UWA's School of Medicine and Pharmacology says thyroid hormone resistance is estimated to occur in one of 40,000 to 50,000 live births.

The X-linked loss of function mutation in the IGSF1 gene described in the study forms a small portion these cases, resulting in hypothyroidism, testicular enlargement, variable prolactin and growth hormone deficiency.

Dr Davis says while the disorder is rare, the new finding is significant for male sufferers living with an underactive thyroid gland and its wide-ranging health impacts like testicular enlargement.

These also include early developmental delay in young children if the defect is severe, to milder forms that could increase the risk of cardiovascular disease in later life.

The multi-national study entitled "Loss-of-function mutations in IGSF1 cause an X-linked syndrome of central hypothyroidism and testicular enlargement" and published in Nature Genetics, involved several generations of 11 unrelated families around the world.

The IGSF1 gene encodes a plasma membrane immunoglobulin superfamily glycoprotein.

Dr Davis says the link to central thyroid resistance, while unexpected, brings a number of benefits to sufferers.

"The finding is important for the individuals in those families affected because they may benefit from screening and perhaps thyroid replacement therapy if the mutation is present," he says.

"Its effects are significant; ensuring normal neurological development in young children and preventing vascular disease in older individuals.

"In addition, it increases our understanding of the complex processes involved in maintaining normal thyroid hormone concentrations and in which the pituitary gland has a vital role, and recognises that such mutations may have effects in tissues other than the thyroid, such as the testes in this case."

Dr Davis says researchers will continue investigating the cellular mechanisms underlying the effects of the IGSF1 mutations on thyroid function.

More information: www.nature.com/ng/journal/v44/ … 12/full/ng.2453.html

Provided by Science Network WA