[CrI] 4.0–15.8) and the mortality would be 34.0% (30.3–39.6). Compared with the base case scenario, halting the increase of diabetes would avoid 6 million incident tuberculosis cases (95% CrI 5.1–6.9) and 1.1 million tuberculosis deaths (1.0–1.3) in these 13 countries over 20 years. If interventions reduce the diabetes incidence by 35% by 2025, 7.8 million (6.7–9.0) tuberculosis cases and 1.5 million (1.3–1.7) tuberculosis deaths could be averted by 2035.

"The diabetes epidemic could substantially affect tuberculosis epidemiology in high-burden countries," the authors write. "The communicable disease and non-communicable disease sectors need to move beyond conventional boundaries and link with each other to form a joint response to diabetes and tuberculosis.

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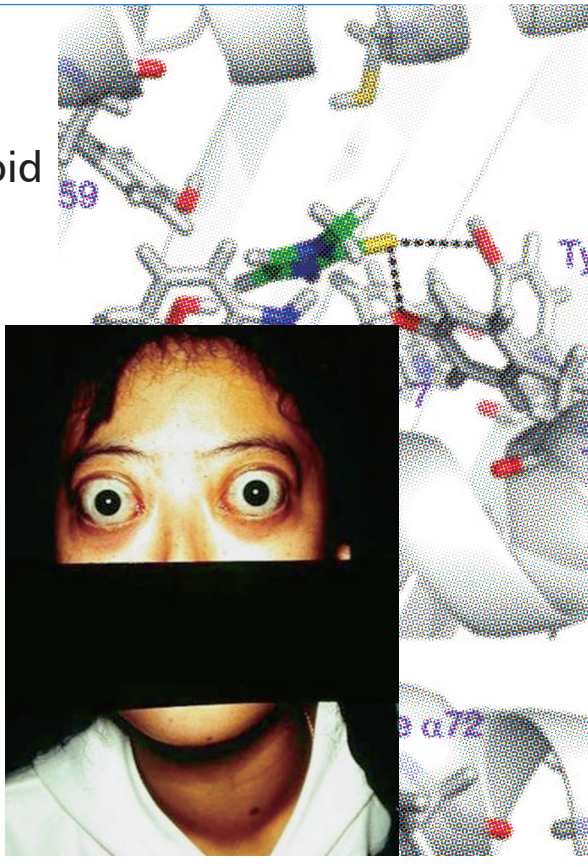
In search of a gene

Two HLA gene loci associated with anti-thyroid drug-induced agranulocytosis



Graves' disease is the leading cause of hyperthyroidism, which affects approximately 1%-1.6% of the general population. Graves' disease primarily results from circulating autoantibodies that target thyroid-stimulating hormone (TSH) receptors on the thyroid gland. After these antibodies bind TSH receptors, the thyroid gland produces and secretes excessive thyroid hormone. Individuals with Graves' disease may present with body weight loss, palpitation, hand tremor, enlarged thyroid gland, and even bulging eyes.

Medical treatment for Graves' disease includes anti-thyroid drugs and radioactive iodine. However, if medical treatment fails, then surgical resection should be considered. Anti-thyroid drugs include methimazole, carbimazole and propylthiouracil, which suppress excessive hormone production by the thyroid gland to achieve clinical remission.

Thus, anti-thyroid agents are the cornerstones of Graves' disease treatment.

However, some patients develop deadly agranulocytosis after treatment with these agents. So-called agranulocytosis, defined as an absolute neutrophil count of less than 500/mm^3, leads to the breakdown of the immune system. Once developed, the risk of severe infection and mortality markedly increases.

Can the onset of agranulocytosis be predicted after administering anti-thyroid drugs?

In July 2015, Professor Chang

and his team published a study concerning the genes associated with anti-thyroid drug-induced agranulocytosis in Nature Communications.

How were the relevant genes identified?

Human Leukocyte Antigen (HLA) should be considered when examining the gene-associated adverse effects of drugs. Located on chromosome 6, HLA shows high variation and is closely associated with immune function, autoimmune disease and some adverse drug effects. In addition, non-HLA genes may affect the metabolism of drugs and have also been associated with the side effects of these compounds.

In this study, direct HLA loci genotyping and a genome-wide association study (GWAS) were employed to analyze genetic differences between individuals with and without agranulocytosis. Direct HLA loci genotyping focuses on differences in HLA alone, whereas GWAS analyzes single nucleotide polymorphisms (SNPs) throughout the entire genome.

These efforts led to the identification of two loci that are highly associated with anti-thyroid drug-induced agranulocytosis: HLA-B*38:02 and HLA-DRB1*08:03. The estimated odds ratios for these two loci, when comparing allele carriers with non-carriers, were 21.48 and 6.13, respectively. Moreover, individuals carrying both HLA-B*38:02 and HLA-DRB1*08:03 show an increased risk of up to 48.41.

These results may guide the decision-making of clinicians in Asia. After diagnosis, doctors can arrange for genetic testing prior to initiating treatments with these compounds. However, when the two HLA loci described above are detected, an alternative treatment should be considered to avoid agranulocytosis.

Reference
Pei-Lung Chen, Shyang-Rong Shih, Pei-Wen Wang, Ying-Chao Lin, Chen-Chung Chu, Jung-Hsin Lin, Szu-Chi Chen, Ching-Chung Chang, Tien-Shang Huang, Keh-Sung Tsai, Fen-Yu Tseng, Chih-Yuan Wang, Jin-Ying Lu, Wei-Yih Chiu, Chien-Ching Chang, Yu-Hsuan Chen, Yuan-Tsong Chen, Cathy Shen-Jang Fann, Wei-Shiung Yang & Tien-Chun Chang. Genetic determinants of antithyroid drug-induced agranulocytosis by human leukocyte antigen genotyping and genome-wide association study. Nat. Commun. 6:7633 DOI: 10.1038/ncomms8633 (2015).

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