Predicting who will react badly to the leprosy drug dapsone

February 26 2014

Credit: AI-generated image (disclaimer)

The antibiotic dapsone is an effective treatment option for leprosy patients. The drug comes with a major safety concern, however: a small, but significant, fraction of the people who take dapsone suffer an adverse reaction that is potentially fatal. While there are currently no assays to help doctors to predict who will develop this so-called dapsone

hypersensitivity syndrome (DHS), a new genetic test could now be on the way thanks to a study led by researchers at A*STAR1.

Jianjun Liu from the A*STAR Genome Institute of Singapore and his colleagues performed a genome-wide association study involving 872 individuals who had received dapsone as part of a multi-drug therapy for leprosy, 39 of whom had experienced DHS. The researchers analyzed more than 430,000 DNA letters scattered across the genomes of the individuals.

Liu and his team identified that a single DNA variant, located in an immunity-associated gene called HLA-B, was significantly more common in those who developed DHS. The team confirmed the finding in two separate cohorts. Pooling across the entire dataset, the researchers observed that the HLA-B*13:01 risk variant was present in 86 per cent of people with DHS and 14 per cent of non-affected controls.

According to the analysis, individuals with one copy of the HLA-B*13:01 variant are 34 times more likely to develop DHS than individuals without this version of the gene. Two copies of HLA-B*13:01 makes individuals 101 times more susceptible to the syndrome. "We can now develop a kit to test the presence of HLA-B*13:01 in patients before dapsone is administered," says Liu. This would "theoretically reduce the risk of DHS sevenfold if implemented in clinical screening."

The HLA-B*13:01 variant is extremely rare in people of European and African ancestry but much more common in people from China and other parts of Asia. Therefore, testing for HLA-B*13:01 would be especially helpful in improving the safety of dapsone drug therapy in Asian populations.

"We are working to develop this test by targeting either HLA-B*13:01

or a proxy marker, and are planning further validations of the test, " says Liu. He adds that, with more than 200,000 new leprosy cases worldwide in 2012, one case of DHS could be prevented for every 84 leprosy patients tested.

Currently, dapsone is administered not just to treat leprosy, but also to combat actinomycosis, pneumonia complications in HIV-infected patients and various chronic inflammatory diseases. Thus, a diagnostic test for DHS risk could have far-reaching health benefits for diverse patient populations.

More information: Zhang, F. R., Liu, H., Irwanto, A., Fu, X.-A., Li, Y. et al. "HLA-B*13:01 and the dapsone hypersensitivity syndrome." *New England Journal of Medicine* 369, 1620–1628 (2013). DOI: 10.1056/NEJMoa1213096

Provided by Agency for Science, Technology and Research (A*STAR), Singapore