

**A Milestone Towards Personalized Medicine in Taiwan**  
**Preventing Adverse Drug Reactions (ADR) with a Gene Test**  
**From post-ADR compensation to preemptive (pre-prescription) prevention**

The Department of Health (DOH) in Taiwan announced today that carbamazepine, a widely used anticonvulsant drug, will carry new information describing a genetic link to the drug's serious side effects. By screening patients before prescription, Taiwan will be first in the world to implement a nationwide ADR prevention program.

According to statistics from our National Reporting System of Adverse Drug Reactions (ADR) in Taiwan, carbamazepine is the number one drug responsible for severe adverse drug reactions such as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis (SJS/TEN). Carbamazepine is an anticonvulsant and mood-stabilizing drug which is used primarily in the treatment of epilepsy and bipolar disorder. It is also used to treat trigeminal neuralgia.

Since 2003, the research team led by Dr. Yuan-Tsong Chen has been conducting retrospective studies for the genetic cause of carbamazepine-induced SJS/TEN. The results showed that the HLA-B\*1502 marker has a very strong association with these serious ADR in Taiwan. Patients who carry the HLA-B\*1502 gene have at least 193 times higher risk of developing ADR than the patients who are not HLA-B\*1502 carriers. Approximately 5% of the Taiwanese population carry the HLA-B \* 1502 gene. Thus, the high frequency is also correlated to the high incidence of CBZ induced SJS/TEN in Taiwan compared to other countries.

Since SJS/ TEN is such a severe and life-threatening adverse drug reaction, often resulting in death or severe disability for an otherwise healthy people, Dr. Sheng-Mou Hou, the Minister of the Department of Health, puts much emphasis on the issue. After assessing the results from many retrospective studies provided by researchers, the Department of Health found the necessity to add the warning onto the labeling of carbamazepine: " Retrospective studies have shown that the human leukocyte antigen HLA-B\*1502 has a very significant association to the carbamazepine induced SJS/TEN. The odds ratio is about 1357 with 95% confidence interval of 193-8838. This means a patient who carries the HLA-B\*1502 gene will have at least 193 times higher risk of developing ADR than a patient who is not a HLA-B\*1502 carrier. Approximately 5% of the Taiwan population carry the HLA-B \* 1502 gene." The purpose of this update in the drug labeling is to bring people's awareness regarding the use of Carbamazepine and the role of genetics in causing drug toxicity.

The discovery on "carbamazepine-induced SJS/TEN, ethnicity-specific and HLA-B\*1502 related gene in ADR" puts Taiwan as a world's leader in pharmacogenetics and personalized medicine in ADR research. . However, due to the

retrospective study design, the clinical application of the results is somewhat limited. Minister Hou believes that the Taiwan government should take the initiative to set the policy for researching toward the personalized medicine. The Department of Health has submitted a "ADR Prevention Program (2008-2012)" to the Executive Yuan, in which the preventive prospective studies to assess the clinical applications of the risk genes will be incorporated, to see if it can effectively reduce the incidence of ADR. Through the implantation of this program, Taiwan's ADR relief system will move from post-ADR compensation to pre-prescription prevention. Taiwan will become the world's first to carry out national wide ADR prevention, and open the doors to personalized medicine.

The Department of Health holds a strict surveillance over domestic and foreign information concerning drug safety and at the same time calls on physicians' attention to take careful assessment of the risks and benefits of treatment before prescribing such drugs to patients. Also, after the treatment, patients' conditions should be carefully monitored. Apart from the National Reporting System of Adverse Drug Reactions in Taiwan (ADR Reporting System), all related information is provided by the "Pharmacovigilance Systems" to protect the public health. When any suspicious symptoms arise while using drugs, patients or medical personnel should immediately communicate the ADR Reporting Systems. ADR Reporting System by phone: 886-2-2396-0100 Website: <http://adr.doh.gov.tw>.