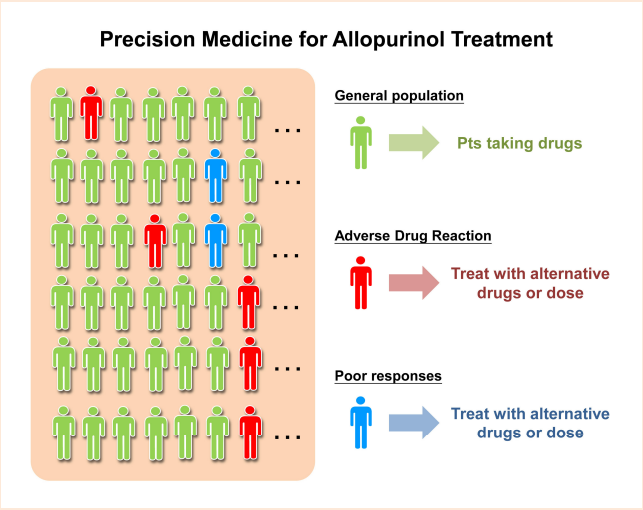
Precision medicine can be a clinical reality: Use of HLA-B*58:01 genotyping to prevent allopurinol induced severe cutaneous adverse reactions in Taiwan

A research team led by Drs. Chen-Yang Shen, Yuan-Tsong Chen and Jer-Yuarn Wu at the Institute of Biomedical Sciences, Academia Sinica completed a large-scale clinical study, demonstrating that the concept of personalized and precision medicine can be a clinical reality, published in the Oct 3rd issue of the British Medical Journal (BMJ).

The development of a reliable pharmacogenomic approach to prevent adverse reactions with severe complications is a major goal of personalized and precision medicine. Severe cutaneous adverse reactions (SCARs) constitute a set of life threatening conditions that include drug rash with eosinophilia and systemic symptoms, Stevens-Johnson syndrome, and toxic epidermal necrolysis, with the lethality rate of toxic epidermal necrolysis at up to 35%. Allopurinol, a first line prescription drug treatment for gout and hyperuricaemia, is one of the most common causes of SCARs in many countries. Although allopurinol has SCARs related risks and other drug treatments for gout are available, allopurinol is still a common treatment for gout and hyperuricaemia owing to its relative low cost, efficacy, and convenience. The research by Dr. Yuan-Tsong Chen has reported previously that allopurinol induced SCARs correlate strongly with the allele human leukocyte antigen (HLA)-B*58:01 in Han Chinese population. This finding has been confirmed in many other Asian populations as well as European populations.

In this study, the research team therefore sought to determine whether prospective screening via HLA-B*58:01 genotyping before allopurinol treatment could reduce the incidence of allopurinol induced SCARs. From July 2009 to August 2014, 2910 participants were enrolled and underwent genotyping. Using information from the National Health Insurance research database of Taiwan, a historical incidence of seven cases of SCARs was predicted among participants receiving allopurinol treatment. In sharp



contrast, in the present study, none of the participants who received allopurinol treatment developed SCARs during follow-up. As a result, prospective screening of the HLA-B*58:01 allele, coupled with an alternative drug treatment for carriers, significantly decreased the incidence of allopurinol induced SCARs in Taiwanese medical centres.

These findings demonstrate potential and significant benefits of genetic testing to prevent adverse drug reactions in proper clinical settings. This pharmacogenomics approach could provide a strong basis for implementation of precision medicine.

The article entitled " Use of HLA-B*58:01 genotyping to prevent allopurinol induced severe cutaneous adverse reactions in Taiwan: national prospective cohort study" can be found at the The British Medical Journal website at:
http://www.bmj.com/content/351/bmj.h4848

The complete list of authors is as follows:

Tai-Ming Ko, Chang-Youh Tsai, Shih-Yang Chen, Kuo-Shu Chen, Kuang-Hui Yu, Chih-Sheng Chu, Chung-Ming Huang, Chrong-Reen Wang, Chia-Tse Weng, Chia-Li Yu, Song-Chou Hsieh, Jer-Chia Tsai, Wen-Ter Lai, Wen-Chan Tsai, Guang-Dar Yin, Tsan-Teng Ou, Kai-Hung Cheng, Jeng-Hsien Yen, De-Ling Liu, Tsung-Hsien Lin, Der-Yuan Chen, Pi-Jung Hsiao, Meng-Yu Weng, Yi-Ming Chen, Chen-Hung Chen, Ming-Fei Liu, Hsueh-Wei Yen, Jia-Jung Lee, Mei-Chuan Kuo, Chen-Ching Wu, Shih-Yuan Hung, Shue-Fen Luo, Ya-Hui Yang, Hui-Ping Chuang, Yi-Chun Chou, Hung-Ting Liao, Chia-Wen Wang, Chun-Lin Huang, Chia-Shuo Chang, Ming-Ta Michael Lee, Pei Chen, Chih-Shung Wong, Chien-Hsiun Chen, Jer-Yuarn Wu, Yuan-Tsong Chen, and Chen-Yang Shen, for the Taiwan Allopurinol-SCAR Consortium