

## Breakthrough in Homogeneous Antibody Development and a New Generation of Glycoarray Technology

A research team led by President Chi-huey Wong and Dr. Chung-Yi Wu, an Associate Research Fellow at the Genomics Research Center, Academia Sinica, in cooperation with CHO Pharma Inc. has developed new homogenous antibodies and a new generation of glycochip technology that is expected to widely influence the field. The research was published in the prestigious journal *Nature Chemistry* (Doi:10.1038/nchem.2463) on March 7, 2016.

Monoclonal antibodies are used to treat a variety of diseases such as cancers, influenza and autoimmune diseases. The pattern of sugar molecules on an antibody (its glycosylation pattern) is crucially important as it affects the antibody's stability, bioactivity, yield, solubility, immunogenicity and so on. The antibody drugs currently available on the market are composed of a mixture of many different sugar structures (glycans). For example, the commercially available anticancer drug Rituxan has a structure that includes 53 kinds of different glycans. The complexity of the glycans on the antibodies makes the manufacturing process complicated and the efficacy of the drugs less than optimal, and also makes the development of antibody and bio-similar drugs difficult.

To overcome the difficulties associated with the heterogeneous nature of antibody drugs, researchers from Academia Sinica Genomics Research Center in collaboration with CHO Pharma have developed homogeneous antibody technology. They use an enzymic reaction to modify the mixture of sugar molecules on antibody drugs into a single homogeneous glycoform, and clarify the optimal glycosylation patterns for different antibodies. This technology can be used to improve current antibodies and new antibodies to target specific glycans on cancer cells. The research results were reported in the US National Academy of Sciences journal, *Proceedings of the National Academy Science (PNAS)*.

<http://www.pnas.org/content/112/34/10611>; <http://www.pnas.org/content/113/4/960>.

However, a bottleneck in homogeneous antibody technology research and development is efficient sugar molecule synthesis. To improve homogenous antibody production, the research team from the Genomics Research Center and CHO Pharma has developed a new modular synthesis method, and also a new generation of glycoarrays. Glycoarrays carry hundreds of different sugars on a chip and are a standard tool for studying the interactions of biomolecules with carbohydrates, including the sugar binding profiles of proteins, knowledge of which is crucially important for the synthesis of therapeutic antibodies. Using the new method, the density of sugar molecules on the glycoarrays is enhanced, and the uneven sugar molecule distribution seen on traditional glycoarrays

is eliminated. Further, the newly developed glycoarrays were able to show that some HIV antibodies isolated from AIDS patients recognized two glycans simultaneously, a trait that could not be detected using traditional arrays. This new discovery will contribute to the development of an AIDS vaccine.

Members of the research team also included one scientist each from the US National Institutes of Health (NIH) and the Scripps Research Institute. The two articles were both co-authored by Academia Sinica President Chi-huey Wong, and Associate Research Fellow, Chung-Yi Wu, at the Genomics Research Center. Academia Sinica has already filed a patent application for the current research, and has granted the exclusive license to CHO Pharma. The company was founded in March 2013 utilizing transfer of glycan engineering technology from Academia Sinica.

The complete list of authors is: Sachin S Shivatare, Shih-Huang Chang, Tsung-I Tsai, Susan Yu Tseng, Vidya S Shivatare, Yih-Shyan Lin, Yang-Yu Cheng, Chien-Tai Ren, Chang-Chun David Lee, Sujeet Pawar, Charng-Sheng Tsai, Hao-Wei Shih, Yi-Fang Zeng, Chi-Hui Liang, Peter D. Kwong, Dennis R. Burton, Chung-Yi Wu and Chi-Huey Wong

The full article, entitled “Modular synthesis of N-glycans and arrays for the hetero-ligand binding analysis of HIV antibodies”, is available at the Nature Chemistry website at:

<http://www.nature.com/nchem/journal/vaop/ncurrent/full/nchem.2463.html>