Deciphering sulfoglycolipids from *Mycobacterium tuberculosis* to elucidate the structure immunomodulatory activity relationship

Janet Jia-Yin Tan,[a] Kwok-Kong Tony Mong[b*] and Chun-Hung Lin[a*]
[a] *Institute of Biological Chemistry, Academia Sinica, Taipei,11529, Taiwan*
[b] *Applied Chemistry Department, National Yang Ming Chiao Tung University, Hsinchu, 30010 Taiwan.*
E-mail: jjtan212@gate.sinica.edu.tw

Mycobacterium tuberculosis (Mtb), the etiological agent of tuberculosis, represents a challenging pathogen because of many casualties worldwide. Sulfoglycolipids (SGLs) are of particular interest to researchers as they are only produced from pathogenic Mycobacterium. SGLs can be further divided into different classes depending on the number, positions, and types of fatty acyl chains (**Figure 1**). Although SGLs are known to have pro-inflammatory activities some of these results were inconsistent. To better understand the structure and immunomodulatory properties of different classes of SGLs, we tested each class of the synthesized SGLs under the same set of experimental conditions. SGLs were tested utilizing a cell line derivative of THP-1 expressing the nuclear factor (NF)-κB-inducible reporter system. Our results showed that SGLs have no NF-κB activation in human THP-1 monocytes. However, SL-IV (**4**) showed inhibitory activity on NF-κB activation when co-incubated in the presence of Pam_3CSK_4, a TLR2/TLR1 agonist that activates NF-κB in THP-1 monocytes. The effect of acyl chain length in SL-IV was also evaluated. Of the three SL-IVs tested, compounds (**4**) and (**7**) with shorter hydroxyphthioceranic (HPA) chain lengths exhibited higher inhibitory activities than (**5**). Molecular docking results supported the possible binding of SL-IV with TLR2 where the binding mode of (**4**) appears to be more convergent than those resulting from (**5**) and (**7**). Overall, our data showed that some of these SGLs display anti-inflammatory activity and the acylation pattern of SGL correlates with the immuno-modulatory property.

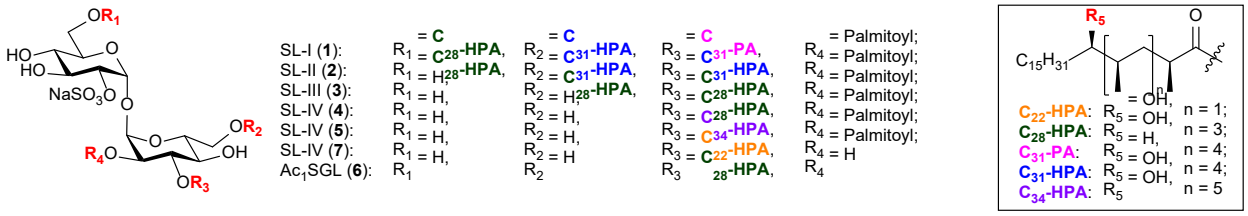

Figure 1 Structure of different classes of sulfoglycolipids.

References

[1] Mondal, S.; Tseng, C. J.; Tan, J.J.Y.; Lin, D. Y.; Lin, H. Y.; Weng, J. H.; Lin, C. H., Mong, K. K. T. *Angew. Chem. Int. Ed.* **2023**, *62*, e202212514.

Janet Jia Yin Tan. Monash University (Bachelor of Science (Honours), 2014), Monash University (Ph.D., 2020, Dr. Yau-Yan Lim), Academia Sinica (Postdoc, 2020-present, Dr. Chun-Hung Lin). Her research interests are related to bioprospecting for novel bioactive compounds with in association with cancers and infectious diseases.