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代表著作：

- Christina Li-Ping Thio, Alan Chuan-Ying Lai, Po-Yu Chi, Gill Webster, **Ya-Jen Chang***, 2019, “Toll-like Receptor 9-dependent Interferon Production Prevents Group 2 Innate Lymphoid Cell-Driven Airway Hyperreactivity”, *Journal of Allergy and Clinical Immunology*, 144(3), 682-697.
- Christina Li-Ping Thio, Po-Yu Chi, Alan Chuan-Ying Lai, **Ya-Jen Chang***, 2018, “Regulation of Type 2 Innate Lymphoid Cell-Dependent Airway Hyperreactivity by Butyrate”, *Journal of Allergy and Clinical Immunology*, 142(6):1867-1883.

簡評：

張雅貞博士的研究主要是聚焦於一種新定義的先天性淋巴細胞（innate lymphoid cells, ILC）在一些重要的免疫疾病，如粘膜炎症和氣喘的病理機制與作用。張博士的研究顯示，來自微生物群的丁酸能夠減少人體 ILC2 的細胞炎症因子生成，而微生物產生的 CpG 序列能夠通過作用於漿細胞樣樹突狀細胞（plasmacytoid dendritic cells）的 toll like recetpor-9 受體和誘導第一型干擾素（type I interferon）的生成來抑制 ILC2 的功能。這些研究極具創新性，並且增進了我們對 ILC2 調節過敏性氣喘所扮演的角色與相關機制的了解，並為設計新的氣喘治療策略，特別是針對重症和重度氣喘提供了必要的基礎。綜合言之，張博士過去幾年的研究表現傑出，代表作在免疫疾病研究領域有重要貢獻，是一位很有前途的年輕科學家，具有出色的才能，未來很有潛力發展為傑出的科學家。

簡歷：

I received my Ph.D. in Pharmacology from the National Taiwan University in 2005. My Ph.D. thesis focused on the mechanism of pathogen-induced inflammation and carcinogenesis at mucosal sites. I went on to do my postdoctoral training at Academia Sinica studying cancer immunology and therapy. To further my interest in the study of innate immunity in infectious and autoimmune diseases, I joined the Boston Children's Hospital, Harvard Medical School in 2008. I have studied the acute influenza virus triggered asthma and identified a new subset of innate lymphoid cells in the lungs. In 2011, I was promoted to the position of instructor in Harvard Medical School. In 2013, I returned to Taiwan and joined the Institute of Biomedical Sciences at Academia Sinica as an Assistant Research Fellow, and was promoted to the Associate Research Fellow with tenure in 2019. Currently, I focus my research on the immunological mechanisms of respiratory infections and asthma, as well as the development of new therapeutic strategy. Specifically, my laboratory is trying to determine how the newly defined innate immune cell subsets (ILC and NKT) regulate the development of asthma and microbial infections, by taking advantage of our mouse models for asthma, as well as being the first to characterize the ILC2s in the lungs. Furthermore, I also want to understand the mechanisms of how ILCs interact with other innate and adaptive immune cells in the pathogenesis of asthma and infectious diseases. These studies will not only reveal how innate immune response profoundly shapes the mucosal immune system of the respiratory tract, but open new areas of research, which may lead to much improved therapies for atopic diseases. Hence, my long-term goals are to understand the roles of innate lymphocytes in asthma, particularly the corticosteroid-resistant type and other allergic diseases, and to develop novel therapeutic applications for targeting these innate lymphocytes.

代表作簡介：

Regulatory Mechanisms to Counteract Group 2 Innate Lymphoid Cell-Driven Airway Inflammation

Background:

Asthma is a chronic respiratory disease characterized by airway hyperreactivity (AHR) and inflammation. Recent studies have identified group 2 innate lymphoid cells (ILC2s) as a critical immune component in driving both allergic and non-allergic asthma development. Moreover, these cells are thought to contribute to steroid resistance. Since corticosteroid-resistant asthma account for up to 10% of asthmatic patients, the significant socioeconomic burden and reduction in life quality for these patients demand the development of new therapeutic strategy.

Approach:

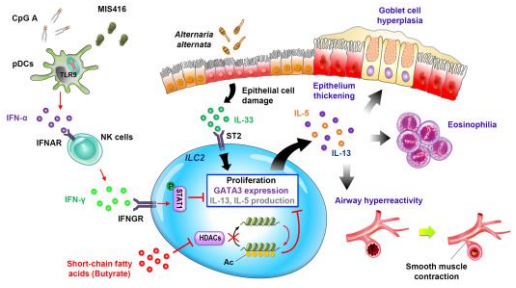
In recent decades, studies have shown that interactions between microbes and their host can modulate host immunity by either triggering or suppressing host immune responses. Thus, we aimed to investigate the effects of microbial metabolites short chain fatty acids (SCFAs) and bacterial CpG DNA on ILC2 activation in the *Alternaria alternata*-driven murine model of fungal allergen-induced asthma.

Outcome:

In a series of studies, we demonstrated that the microbial metabolite butyrate could suppress ILC2 cell proliferation, GATA3 expression, and cytokine production through the inhibition of Histone deacetylases (HDAC) (JACI, 2018). We also showed that CpG A could activate Toll-like receptor 9 (TLR9) and inhibit ILC2-driven AHR and inflammation through plasmacytoid dendritic cell (pDC)/IFN-α/NK cell/IFN-γ axis. Extending on the CpG A result, we further showed that the CpG-containing microparticle derived from *P. acnes* (MIS416) could serve as a potential treatment for asthma (JACI, 2019).

Significance:

Collectively, these findings reveal important regulatory mechanisms to counteract ILC2-driven airway inflammation, which may pave way for the development of new therapeutics to prevent or treat steroid-resistant asthma.



得獎感言：

我很榮幸能進入中研院生物醫學科學研究所，帶領優秀的實驗室團隊進行氣喘與過敏機轉的研究，一切研究成果都是歸屬於這個團隊努力。一路走來雖有挑戰與挫折不斷，但同時也獲得許多學研前輩的提攜與勉勵，我心存感恩。我最感謝家人的支持，尤其是我在天上的父母，以及一路相挺的先生，還有我兩個可愛的小寶貝，他們讓我要不斷努力學習如何有效率地完成工作同時當稱職的媽媽。我期許我們團隊的研究，未來能對氣喘的預防與治療有所貢獻。