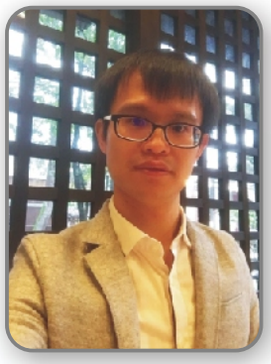

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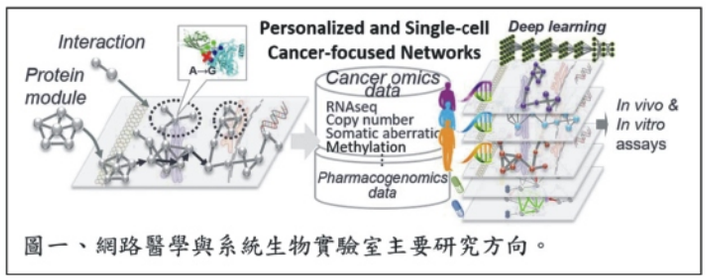
研究興趣



圖一、網路醫學與系統生物實驗室主要研究方向。

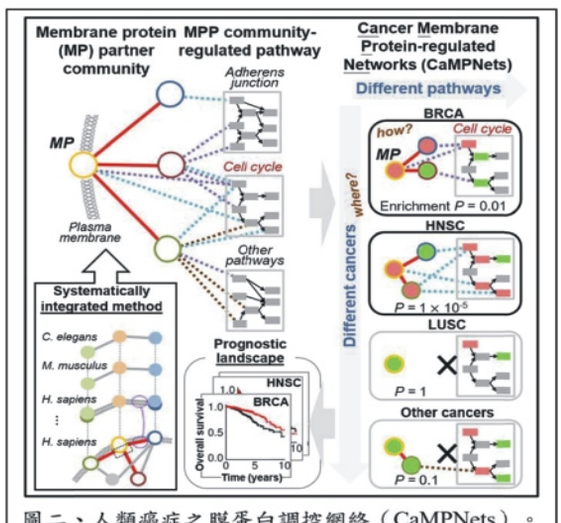
網路醫學與系統生物實驗室 (MedSB.net) 致力發展以生物網路 (Biological Networks) 結合多體學 (Multi-omics) 資料來建構疾病調控網路模型，透過比對分析患者群體、單一患者個體 (Patient-specific)、乃至單細胞 (Single-cell) 和藥物基因組學 (Pharmacogenomics) 所建立之網路模型，我們專注於研發次世代精準醫療檢測技術及臨床治療決策的輔助工具。主要研究成果如下：

• 蛋白質間交互作用、蛋白質模組及生物網路

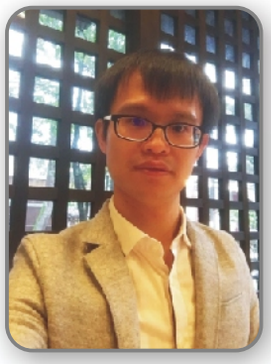
隨著各種組學資料(Omics data)的快速增長，如何整合這些資料與生物網路來探討疾病機制成為當前的重要課題。然而，兩個核心問題尚未被解決—絕大部分物種之交互作用體(Interactomes)並不完整；靜態的網路無法反映細胞內的變動。為了解決上述問題，我們過去已發表多項新概念及新技術，例如：蛋白質間交互作用家族(PPI family；發表於*Nucleic Acids Research, 2009*)和蛋白質模組家族(MoNetFamily；發表於*Nucleic Acids Research, 2012*)。這些方法透過映射不同物種之交互作用實驗資料於特定物種，可精準預測蛋白質間交互作用、蛋白質模組及模組間交互作用，進而模擬真實細胞內的生物網路。此外，透過必要基因分析、模組變化分析及大規模基因共表現分析，我們成功發現蛋白質模組在生化網路的組成原則及變動行為。(發表於*Scientific Reports, 2015*)，該成果有助於生物學家找出細胞在特定狀態下（如癌症）的關鍵基因及潛在藥物標靶。

• 計算腫瘤學及臨床診斷/治療之開發

至今，我們已應用所發展之概念及方法與國內外數個頂尖研究機構及公司合作進行臨床癌症研究，包含日本京都大學、澳洲Monash大學、Nvidia AI Technology Center (日本及新加坡)與台北醫學大學。例如，我們與北醫共同發展一個系統化整合計算模型，透過分析15種癌症5,922腫瘤基因表現資料及臨床資訊，大規模針對2,594個人類膜蛋白預測並建立其癌症膜蛋白調控網路(發表於*Nature Communications, 2019*)，可進一步用於探討癌症同質/異質性及發展15種癌症的預後生物標記組與藥物標靶蛋白；我們更透過此系統成功找到一個新穎抑制劑(舊藥新用；美國專利申請中)，可有效抑制乳癌轉移發生。此外，我們與日本NVIDIA公司共同合作透過深度學習(Deep Learning)開發AI 智慧演算模型，藉由分析腫瘤基因體大數據資料發展癌症亞型精準檢測技術，可應用於患者癌症亞群及單細胞分類甚至是臨床資訊預測(發表於*Journal of Bioinformatics and Computational Biology, 2019*)。



圖二、人類癌症之膜蛋白調控網絡（CaMPNets）。



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Research Interests

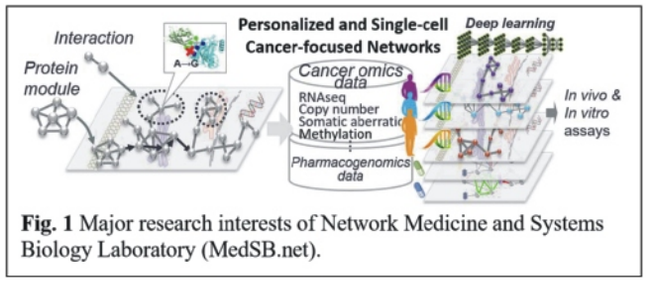

Fig. 1 Major research interests of Network Medicine and Systems Biology Laboratory (MedSB.net).

Laboratory of Network Medicine and Systems Biology (MedSB.net) aims to integrate multi-omics data with the biological networks for establishing disease-focused regulatory network models. Via the comparative analysis of networks for bulk and individual patient data, single-cell data, as well as pharmacogenomics data, we focus on the development of the next-generation diagnostics and the clinical decision support systems. Some research achievements are described as follows:

Protein-protein interactions, protein modules, and biological networks

As an increasing number of various omics data become available, there is a growing need to integrate these data with the biological networks to reveal disease mechanisms. Nevertheless, two open issues remain challenging. First, the interactomes in most of the organisms are still incomplete. Second, the static networks cannot reflect the variations in cells. In support of these pursuits, we have proposed the novel concepts of "PPI family (***Nucleic Acids Research, 2009***)" and "module family (***Nucleic Acids Research, 2012***)" to map the verified PPIs and module-module interactions (MMIs) from multiple species to target species (called homologous mapping) for efficiently enlarging high-quality PPIs/MMIs and for simulating close-to-real biological networks in cells. Based on the analyses of gene essentiality, module variance, and gene co-expression, we are the first study to summarize the observations of module organization and variance in biological networks (***Scientific Reports, 2015***). This observation is useful to identify key genes of cells in certain abnormal conditions (e.g., cancers) and discover the potential druggable targets.

Computational oncology and clinical diagnosis /therapy development

Up to now, we have applied our developed concepts and methods to collaborate with several remarkable research institutes/industries for clinical cancer research, including Kyoto University (Japan), Monash University (Australia), Nvidia AI Technology Center (Japan and Singapore), and Taipei Medical University (TMU, Taiwan). For example, we collaborated with TMU to develop a systematically integrated method (SIM) to generate a resource of Cancer Membrane Protein-regulated Networks (CaMPNets) using expression profiles from 5,922 tumors with overall survival outcomes across 15 types of human cancer (***Nature Communications, 2019***). This study investigated "membrane proteins (MPs)" on a large scale to systematically integrate MP interactions, genomics, and clinical outcomes to illuminate cancer-wide atlas and prognostic landscapes in tumor homo/heterogeneity and inform novel biological and diagnostic/therapeutic strategies. By using CaMPNets, we identified a repurposed drug (***U.S. patents pending***), as a new anti-metastatic agent for treatment in nicotine-induced breast cancer. Additionally, we also collaborated with the Nvidia AI Technology Center in developing a feature-based convolutional neural network (CNN) strategy and an image-based strategy (***Journal of Bioinformatics and Computational Biology, 2019***), and these strategies could be applied to patient/single-cell classification and clinical information prediction.

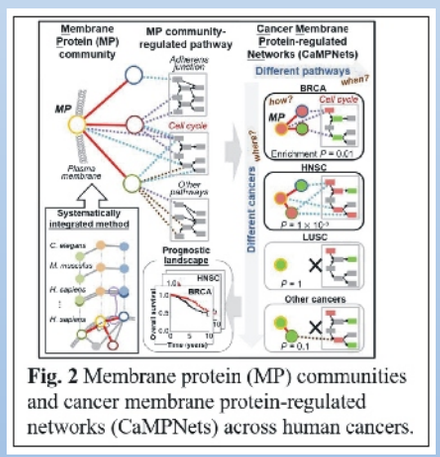

Fig. 2 Membrane protein (MP) communities and cancer membrane protein-regulated networks (CaMPNets) across human cancers.