Dr. Mary Chang's Lab

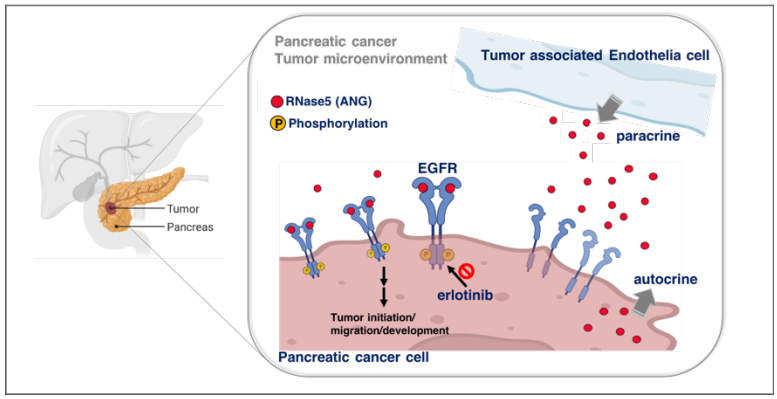
Dr. Mary Chang's lab is dedicated to the functional and structural studies of biologically essential proteins in fundamental biology. By employing integrative tools, including X-ray crystallography, Cryo-EM, biophysical, biochemical, and cellular based methods, the lab determines and dissects the 3D protein structures to address how the protein functions and interacts with its binding partners, such as small compound and protein. Her research aims to combine basic and translational research to uncover potential therapeutic targets for treating cancer and infectious diseases. By developing small compound or antibody drugs with her collaborators, she hopes to provide effective cures that are helpful for patients.

The theme of her research focuses on exploring the molecular basis of cell-cell communication, particularly for the cells in relevant to pathogenicity, such as cancer cell, immune cell, and infectious micro-organisms (bacteria, fungi, and virus). The biomolecular interactions which are often crucial to cellular function, and thus the malfunction or imbalance of the molecular cross-talk ultimately leads to pathogenicity. She actively establishes local and international collaborations with scientists specialized in Cancer, Immunology, Microbiology, Drug screening, Synthetic Biology and Computational biology to deepen the scope of her research subjects, as well as to develop the new therapeutic strategies targeting human cancer and infectious diseases.

The Silent talk that Matters

The main focuses on cell-cell communication *via*: **1.** protein ligand; **2.** small molecule (metabolite)

1. **Signaling transduction in cancer**
   - Receptor Tyrosine Kinase-RNase5 axis-directed therapeutics innovation for pancreatic cancer treatment.

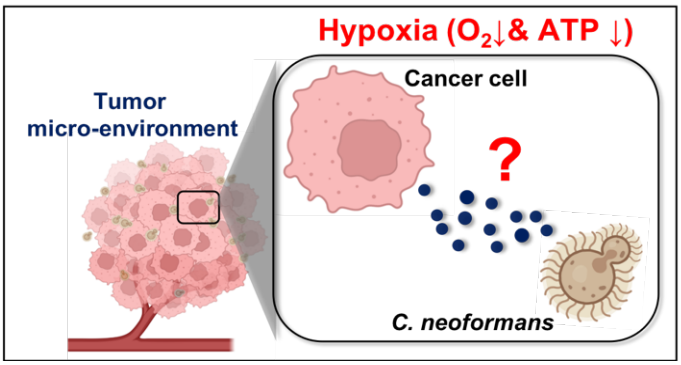


RNase5 (Angiogenin, ANG) is an EGFR ligand and a serum biomarker for erlotinib sensitivity in pancreatic cancer (*Cancer Cell* **33**, 752-769 e758, 2018). RNase5 binds to EGFR and triggers downstream signaling cascades, which are sensitive to erlotinib, a tyrosine kinase inhibitor[5]. The figure was prepared using BioRender.com.

2. **Cancer microbiota: Metabolic interplay between cancer cell and human pathogens**
   - Molecular basis of the metabolic cross-talk between host and fungi: Strategies

for anti-fungal development and suppressing tumorigenesis.

Fungal microorganisms (mycobiota) comprise a small but non-negligible component of the human micro-biome, which closely correlate with tumorigenesis, cancer progression, immunogenicity and response to therapy. Pan-cancer analyses revealed tumor-associated mycobiomes at multiple body sites yet how fungi is involved in these carcinogenesis process and the conclusive link with cancer still remain largely unexplored. The molecular basis of the metabolic crosstalk between the fungal and cancer cells will be necessitated to provide innovative approaches of managing invasive fungal infection, and concurrently eliminating tumorigenesis. The emergence of resistance to antifungal drugs has challenged human health systems globally. The characteristics and management of such host-pathogen interplay need further investigation in particular immune-compromised patients. Therefore, the research objective is to explore the molecular basis of host-pathogen interplay for developing novel dual-functional therapeutics not only to conquer an invasive fungal pathogen, *Cryptococcus neoformans (C. neoformans)*, but also to dampen cancer progression in cancer patients who suffer from cryptococcosis.



The hidden link between fungal infection and cancer. The metabolic interplay between cancer cells and *C. neoformans* under hypoxic tumor-microenvironment. Figure was made by using BioRender.com.

Dr. 張瓊文(Mary Chang)實驗室致力於利用生物化學，生物物理及結構生物學技術 (x-ray 蛋白晶體繞射及冷凍電子顯微鏡)，來探討並解析蛋白質特質及3D 立體結構。同時亦積極從事轉譯醫學研究，尋找治療癌症或感染性疾病的標靶，·並開發設計專一性藥物，希望未來能夠對病患有所助益。

目前研究的主題為探討細胞間的溝通途徑及方式。尤其是跟病理相關的細胞，如癌細胞、免疫細胞及致病性微生物細胞(microbiome) 包括: 細菌、黴菌及病毒。我們也積極與癌症及微生物研究團隊建立合作關係，來加深對研究主題的了解並進一步發展相關治療策略。

目前主要計畫分別針對細胞主要溝通媒介中的 (1)protein ligand 及(2)代謝小分子(metabolite)來做探討：

(1) Receptor Tyrosine Kinase-RNase5 axis-directed therapeutics innovation for pancreatic cancer treatment.

本計畫是來探討 RNase5 如何扮演 protein ligand 的角色來活化 receptor tyrosine kinase family 中的一員 (EGFR），在先前研究中發現胰臟癌病人血清中存在過量的 RNase5，並且 RNase5對 EGFR 具有專一性的結合，並過度活化其相關細胞內的訊息傳導途徑及蛋白分子，然而其活化機制尚未被探討。

(2) Molecular basis of the metabolic cross-talk between host and fungi: Strategies for anti-fungal development and suppressing tumorigenesis.

真菌是人類微生物體中不可忽視的組群之一，它與腫瘤發生、癌症發展、免疫原和治療反應密切相關。近期泛癌症研究揭示了真菌與身體多個部位的腫瘤發展有關聯，但真菌如何參與腫瘤癌化過程以及關聯程度仍未被探討。而且抗真菌藥物抗藥性已經給全球人類衛生系統帶來了挑戰。有關宿主及病原體的相互作用及影響也需要進一步研究。所以此計畫目的：探討在致病性感染或腫瘤微環境下（低氧和缺乏細胞能量 ATP），侵入性真菌病原體：新型隱球 Cryptococcus neoformans，和癌細胞之間的代謝相互作用。

歡迎對研究及研發有興趣的學生，助理及博後加入 Dr. Mary Chang's lab.