發展anti- CD33 (Siglec-3)抗體以治療慢性B型肝炎及阿滋海默症

主要領域 感染性疾病

- 產品/技術簡介
  - CD33 (Siglec-3)為具有免疫酪胺酸抑制模體(ITIM)的骨髓細胞受體(myeloid membrane receptor)，與免疫檢查點受體PD-1相似。我們近期的研究發現CD33為B型肝炎病毒之模式識別受體，且B型肝炎病毒經由CD33傳遞抑制訊息以壓制宿主免疫。我們亦發現CD33- rs12459419C等位基因(CD33高度表現)與B型肝炎病患中發生肝癌的高風險群有密切關聯。我們更進一步生產anti-CD33拮抗性單株抗體，發現其能引發慢性B肝患者的血球細胞產生anti-HBsAg抗體，顯示anti-CD33抗體(SP-1)可突破HBV造成的免疫耐受性，可激活病人的免疫力清除HBV而達到"治療"慢性B型肝炎的目標。新型的anti-CD33抗體(SP-2)可激活腦部的microglia，清除β-amyloid及胞外的Tau蛋白。Alector/Abbvie已利用anti-CD33抗體申請臨床試驗治療阿茲海默症，顯示SP-2抗體具有極大潛力可治療阿茲海默症的效益。

- 應用
  - SP-1抗體激活慢性B肝炎病人免疫力以產生抗HBsAg抗體，清除B 型肝炎病毒。
  - SP-2抗體活化微膠細胞，增強清除β澱粉樣蛋白的能力。
- 優勢
  - 目前沒有任何抗CD33單株抗體，能阻斷HBV的免疫抑制
  - SP-1抗體與anti-PD-1抗體有加成效果，可強化anti-PD-1之抗癌作用
  - 目前沒有任何抗CD33單株抗體，能增強巨噬細胞/微膠細胞的吞噬能力。
- 專利現況
  - 已針對抗CD33抗體組成以及治療B型肝炎和阿茲海默症之應用申請國際專利。

Development of Anti- CD33 (S iglec-3) mAb for the Treatment of Chronic Hepatitis B Infection and Alzheimer Diseases

Research Area Infectious Disease

- Technical statement
  - CD33 (Siglec-3) is a myeloid membrane receptor which contains an immunoreceptor tyrosine-based inhibitory motif (ITIM) similar to the immune checkpoint receptor PD-1. We found that CD33 as a pattern recognition receptor to hepatitis B virus (HBV), and generated antagonistic anti-CD33 mAb (SP-1) to induce anti-HBsAg antibody using the PBMCs from chronic hepatitis B patients, indicating SP-1 mAb is able to break HBV-induced immune tolerance. We further generated high affinity human antibodies against CD33, and found that the anti-CD33 mAb (SP-2) can activate microglia to uptake beta-amyloid and extracellular hyperphosphorylated Tau protein. Alector/Abbvie has launched phase I clinical for the safety of anti-CD33 mAb in Alzheimer's disease (AD), and suggesting SP-2 antibodies has great potential to be become therapeutic agent for the treatment of AD..
- Applications
  - SP-1 mAb can be applied for the treatment of chronic hepatitis B.
  - SP-2 mAb has great potential to become therapeutic antibodies for HBV.
- Advantages
  - The proprietary SP-1 mAb is the sole mAb which is show to reactivate host immunity to break HBV-mediated immunosuppression.
  - SP-1 mAb can enhance anti-PD-1 mAb to enhance host immunity against chronic viral infection and cancer.
  - The proprietary SP-2 mAb is able to actovate microglia to clear beta-amyloid and hyperphosphorylated Tau peptide..
- Patent status
  - We have filed patents for the composition of anti-CD33 mAbs, as well as its application to treat CHB and AD.

計畫主持人 Project PI

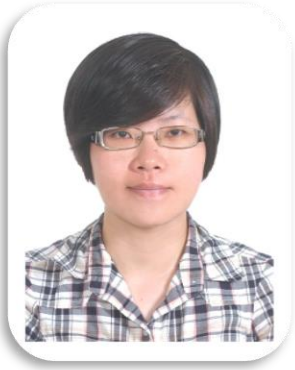
謝世良
Shie-Liang Hsieh

- **Website:** https://www.genomics.sinica.edu.tw/index.php/tw/hsieh-shie-liang
- **Contact person:** Tso-Yu Chou
- **TEL:** +886-2-2789-8813
- **Email:** tychou@gate.sinica.edu.tw
  wu@gate.sinica.edu.tw

計畫成員 Member

宋佩珊

彭裕淳



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