

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

## 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 $\beta$ -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型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 $\beta$ 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 (Siglec-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 activate 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.

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