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特許申請・取得

- 特願2011-287603 「IL-28Bの分析方法」 溝上雅史、杉山真也、木村達治
- PCT/JP2011/79353 「B型肝炎ウイルス群を検出し、遺伝子多様性を評価するためのオリゴヌクレオチドのセット、並びにそれを用いた方法」 溝上雅史、杉山真也、新井 理、田村卓郎
- 特願2011-211647 「C型肝炎患者の経過予測方法」 溝上雅史、杉山真也
- 特願2010-063622 「C型肝炎の治療効果を予測するためのマーカー群、検査方法及び検査用キット」 溝上雅

史、田中靖人、徳永勝士

5. 特願2009-192615 「C型肝炎の治療効果を予測するためのマーカー及びC型肝炎の治療効果の予測を行う方法並びにC型肝炎の予防又は治療剤」溝上雅史、田中靖人、徳永勝士
6. 特願2009-287243(特願2009-165795) 「糖タンパク質の測定方法、肝疾患の検査方法、糖タンパク質定量用試薬および肝疾患病態指標糖鎖マーカー糖タンパク質」溝上雅史、伊藤清顧、成松久ほか、田中靖人、松原俊介ほか
7. 特願2009-165795 「肝疾病病態診断指標糖鎖マーカー」溝上雅史、成松久ほか、田中靖人

平成25年度厚生労働科学研究費補助金(B型肝炎創薬実用化等研究事業)研究発表会
平成26年1月30日

「人工キメラ遺伝子と肝臓特異的な輸送担体の開発を基盤とした
肝臓内HBVDNA不活化を目指した新規治療法の開発」(溝上班)
(H24-B創-肝炎-一般-011)

平成25年度進捗状況と次年度計画

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研究分担

目的
肝細胞核内のHBVゲノムの不活化・排除

人工キメラ遺伝子
Zinc Finger Nuclease (ZFN)
TAL Effector Nuclease (TALEN)
CAS9/CRISPR
(溝上、杉山、福原、安井)

+
デリバリー・システム開発
高分子ノゾドバイス
非ウイルスベクター
肝臓特異的取り込み分子
(片岡)

in vitro, in vivo実験モデル
cccDNA, Integrated HBV DNA模倣系
(杉山、福原、安井)

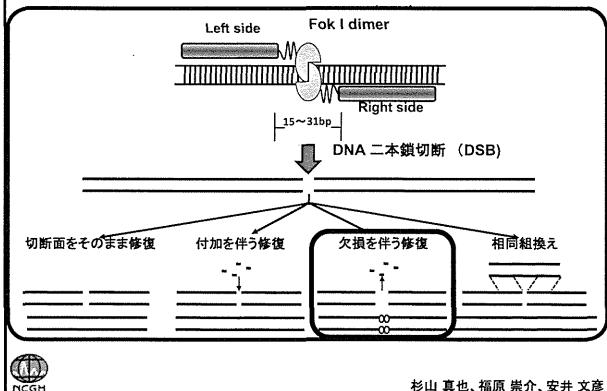
輸送分子の安定化
分子の安定化、分解調節
(星野)

副作用の検証
全ゲノムシーケンス
(杉山)
二本鎖DNA切断(DSB)
(中西)

ex vivo検査
患者由来組織でRNの検証
(田中、武富)

→ 臨床試験フェーズ1
(助水:協力研究者)

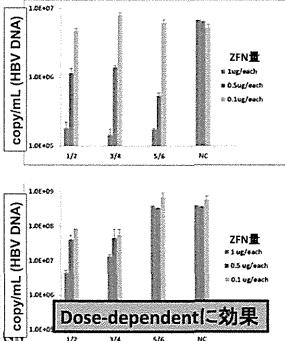
人工キメラ遺伝子(核酸-蛋白結合型)



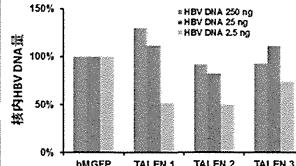
杉山 真也、福原 崇介、安井 文彦

核酸-蛋白結合型人工遺伝子の切断活性

最適化後のZFNによるHBV DNA切断活性



最適化後のTALENによるHBV DNA切断活性

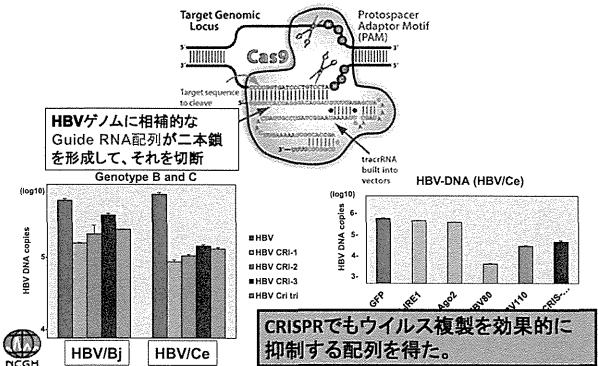


ZFN, TALENの最適化により、ウイルス複製を効果的に抑制する配列を得た。

杉山 真也、福原 崇介、安井 文彦

人工キメラ遺伝子について(核酸-核酸結合型)

HBVゲノムを標的とするCRISPR/Cas9による抗HBV活性



mRNAのナノミセル型輸送担体の開発と機能解析

DNAはゲノムへの挿入の危険性
→表現が制御できなくなる
より安全なmRNAを使用

mRNAをナノミセル型輸送担体へ内包

mRNA
DNA
細胞
核

mRNA
細胞
核

mRNA治療の問題点
・体内ですぐに分解
・免疫反応を誘導

mRNA
細胞
核

生体への応用は不可能であった

mRNA
細胞
核

肝臓へのルシフィラーゼ発現 mRNAの投与

mRNA
細胞
核

mRNA
細胞
核