

厚生労働科学研究費補助金（肝炎等克服緊急対策研究事業）  
分担研究報告書（平成 23 年度）

B型肝炎ウイルス感染の病態別における宿主因子等について、網羅的な  
遺伝子解析を用い、新規診断法及び治療法の開発を行う研究

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分担研究課題：ウイルスマーカーの臨床的有効性評価

研究要旨：全国多施設共同研究により、HBs抗原陽性の肝がん患者79例と、年齢を一致させた非肝がん患者（無症候性キャリア、慢性肝炎）77例をコントロールとして、ウイルス遺伝子解析を行った。結果：男性の割合、genotype Cの割合、C1653T変異及びA1762T/G1764A変異が肝がん患者で有意に高かった( $p<0.01$ )。これらは、従来から肝がんとの関連性が報告されているウイルス変異で、今後は宿主因子と組み合わせることで、より精度の高い診断が期待される。

#### A. 研究目的

本研究班の目的は、B型肝炎ウイルス感染に起因する各種の病態形成に関わる宿主（ヒト）因子を網羅的ゲノム解析により同定し、新たな診断法や治療法の開発に寄与することにある。分担研究として、同一個体内でのウイルスゲノムの解析や遺伝子機能解析も実施することにより、各種病態形成に関わる宿主遺伝要因間や宿主遺伝要因とウイルス因子間の相互作用も明らかにすることである。

#### B. 研究方法

全国多施設共同研究により、検体とその検体についての臨床データおよび患者様情報（付帯情報）の収集を行った。各施設において検体とデータは、連結可能な匿名化を行った上で提出頂いた。HBs抗原陽性の肝がん患者79例検体と、年齢を一致させた非肝がん患者（無症候性キャリア、慢性肝炎）77例をコントロールとして、検体を採取、DNA抽出、ウイルス遺伝子配列を決定し、肝がん特異的変異の有無を検索した。

（倫理面への配慮）

ヒト由来試料の解析にあたり、新規試料については必ずインフォームドコンセントを取得し、既存試料についてはインフォームドコンセントの取得されたもののみを取り扱い、解析データの公表に際しては個人情報保護を徹底する。

#### C. 研究結果

HBs抗原陽性の肝がん患者79例と、年齢を一致させた非肝がん患者（無症候性キャリア、慢性肝炎）77例をコントロールとして、ウイルス遺伝子解析を行った。Genotype Cの割合、C1653T変異及びA1762T/G1764A変異が肝がん患者で有意に高かった( $p<0.01$ )。

#### D. 考察

従来から報告されているC1653T変異及びA1762T/G1764A変異が肝がん患者で有意に高かった。今後は宿主因子と組み合わせることで、より精度の高い診断が期待される。

#### E. 結論

今回の日本人集団において、肝がんに関連するウイルス変異が同定された。

F. 研究発表

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G. 知的所得権の出願・登録状況

1. 特許取得  
なし
2. 実用新案登録  
なし
3. その他  
なし

### III. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻・号	ページ	出版年
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\*IV.研究成果の別刷あり

#### IV. 研究成果の刊行物・別刷