

厚生労働科学研究費補助金（第3次対がん総合戦略研究事業）  
分担研究報告書

多発性大腸腫瘍患者の発がん予防

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本邦では大腸癌の罹患が急激に増加しているため、大腸癌発生を予防する方法の開発が急がれる。これまでも、食生活指導、食品成分の投与などによる臨床試験を行ったが、大腸癌予防効果は比較的軽度である。そこで今回は、低用量アスピリン腸溶錠を用いたより強い大腸癌予防法の開発を研究の目的とした。割り付けは、層別化ブロックランダム法を採用し、試験参加者は、組織診断で確診された大腸腫瘍（粘膜内癌・腺腫）を1個以上持ち、それらすべてを内視鏡的に摘除できた40歳以上、70歳以下の者である。試験薬としてアスピリン（100mg/day）腸溶錠またはプラシーボ錠を用い、主エンドポイントは、2年目の大腸内視鏡検査における新たな大腸腫瘍の発生の有無である。700名の試験参加、500人の解析対象者を目標としているが、2006年7月に試験開始、2009年12月に終了する予定である。大腸癌化学予防のため、低用量アスピリン腸溶錠（100mg/day）の効果を評価する臨床試験実施の準備が整った。

A. 研究目的

本邦では大腸癌の罹患が急激に増加しているため、大腸癌発生を予防する方法の開発が急がれる。これまでも、われわれは食生活指導、食品成分の投与などによる臨床試験を行い、多くの大腸癌予防に関する知見を得てきたが、それらによる予防効果は比較的軽度である。そこで今回は、低用量アスピリン腸溶錠を用いたより強い大腸癌予防法の開発を研究の目的とした。

B. 研究方法

試験参加者は、組織診断で確診された大腸腫瘍（粘膜内癌・腺腫）を1個以上持ち、それらすべてを内視鏡的に摘除できた40歳以上、70歳以下の者である。割り付けは、層別化ブロックランダム法を採用する。試験薬はアスピリン（100mg/day）腸溶錠またはプラシーボ錠である。主エンドポイントは、2年目の大腸内視鏡検査における新たな大腸腫瘍の発生の有無である。副エンドポイントは、試験期間内の有害事象発生率、他臓器癌の発生の有無、2年目の大腸内視鏡検査における新たな大腸腫瘍の大きさ・個数・組織（異型度、絨毛状腺腫成分の有無）、介入後2～3年後の大腸腫瘍発生状況、直腸粘膜のACF数、S状結腸粘膜の大腸癌関連蛋白のmRNA発現

程度である。700名の試験参加、500人の解析対象者を目標とする。

（倫理面への配慮）

本研究は、厚生労働省や関連省庁等が示す指針に従って実施する。参加呼びかけは面接により行い、インフォームドコンセントを得て書面により記録を残す。個人情報保護に十分配慮する。

C. 研究結果

頻回のメール会議と2回の全体会議によりプロトコルを作成し、倫理モニタリング委員会に申請、承認を得て、参加施設への倫理委員会申請手続き中である。試験薬（低用量アスピリン腸溶錠、プラシーボ）はバイエルドイツ本社より輸入し、1シート31錠PTP両面アルミ包装を行った。2006年7月に試験開始、2009年12月に終了する予定である。

D. 考察

頻回のメール会議と2回の全体会議によりプロトコルを作成し、倫理モニタリング委員会に申請、承認を得て、参加施設への倫理委員会申請手続き中である。試験薬（低用量アスピリン腸溶錠、プラシーボ）はバイエルドイツ本社より輸入し、1シート

31錠P T P両面アルミ包装を行った。

2006年7月に試験開始、2009年12月に終了する予定である。本試験で低用量アスピリン腸溶錠の大腸腫瘍抑制効果が明らかになれば、大腸癌高危険群に長期間投与する大規模コホート研究などにより、大腸癌発生予防効果を評価する研究に進むことができるであろう。

#### E. 結論

大腸癌化学予防のため、低用量アスピリン腸溶錠(100mg/day)の効果を評価する臨床試験実施の準備が整った。

#### G. 1 論文発表

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H. 知的財産権の出願・登録状況  
(予定を含む。)

特許出願

なし

実用新案登録

なし

その他

なし

研究成果の刊行に関する一覧表

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Shoji, Y., Takahashi, M., Takasuka, N., Niho, N., Kitamura, T., Sato, H., Maruyama, T., Sugimoto, Y., Narumiya, S., Sugimura T, and <u>Wakabayashi, K.</u>	Prostaglandin E receptor EP3 deficiency modifies tumor outcome in mouse two-stage skin carcinogenesis.	Carcinogenesis	26	2116-2122	2005
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研究成果の刊行に関する一覧表

雑誌

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Kawai, N., Ito, A., Nakahara, Y., Futakuchi, M., <u>Shirai, T.</u> , Honda, H., Kobayashi, T. and Kohri, K.	Anticancer effect of hyperthermia on prostate cancer mediated by magnetite cationic liposomes and immune-response induction in transplanted syngeneic rats.	Prostate	64	373-381	2005

研究成果の刊行に関する一覧表

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
<u>Tanaka, T.</u> , Suzuki, R., Kohno, H., Sugie, S., Takahashi, M. and <u>Wakabayashi, K.</u>	Colonic adenocarcinomas rapidly induced by the combined treatment with 2-amino-1-methyl-6-phenylimidazo[4,5- <i>b</i> ]pyridine and dextran sodium sulfate in male ICR mice possess $\beta$ -catenin gene mutations and increases immunoreactivity for $\beta$ -catenin, cyclooxygenase-2 and inducible nitric oxide synthase	Carcinogenesis	26	229-238	2005
Sugie, S., Ohnishi, M., Ushida, J., Yamamoto, T., Hara, A., Koide, A., Mori, Y., Kohno, H., Suzuki, R., <u>Tanaka, T.</u> , <u>Wakabayashi, K.</u> and Mori, H.	Effect of $\alpha$ -naphthyl isothiocyanate on 2-amino-3-methylimidazo[4,5- <i>b</i> ]pyridine (PhIP)-induced mammary carcinogenesis in rats.	Int. J. Cancer	115	346-350	2005
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