第92回 米国癌学会

■2001年3月24日～28日　米国ルイジアナ州・ニューオリンズ

#4334

「Tumor initiating Effects of Nitric Oxide Donors in Two-Stage Mouse Skin Carcinogenesis and its Prevention.」

マウス皮膚二段階発がんにおける一酸化窒素の作用と予防

Harukuni Tokuda, Masato Okuda, Masato Kutidi, Teruo Mukainaka, Hoyoku Nishino,
Takao Konoshima,and Midori Takasaki. Dopt.of Biochmistry, Kyoto Prefectural University of Medicine, Kyot, Japan
Kyoto Pharmacoutical University, Kyoto, JAPAN. And Kyoto Prefectural University of Medicine, Kyoto, Japan.

Nitric oxide (NO) plays an important role in number of physiological functions. Hence NO may be useful for treatment of several diseases. But NO is also a mutagen and can cause mutations in both microorganisms and mammalian cells. To examine the possible role of NO induced carcinogenesis, we tested the effects of NO donors, new type NO donors, S-Nitrosothiol and Peroxynitrite (PN) in two-stage mouse skin carcinogenesis. Female SENCER mouse (6weeks of age) were treated topleally with single dose of PN solution followed by TPA twice a weekly for 20 weeks. Tumor incidences were 1OO% with 5 to 6 papillomas per mouse at and of experiment, To characterize genetic events during nitric oxide induce carcinogenesis, papillomas DNA was extracted and H-ras axons were amplified by PCR for analysis of H-ras 61 codon mutation.
This leads to elevated levels of activated ras gone, contributing to their production of H-ras mutation correlate with induction of PN tumor initiating effect and/or an important early overts in carcinogenesis And naturally occurring materisis (curucumin etc.) inhibit NO induced tumor initiation, these effects of naturally occurring compounds that they may be useful prevention against NO induced damage.

■日本語訳

一酸化窒素（NO）は多くの生理活性を有し、重要な役割をしている。

このことからNOは種々の疾患の防御に、有用な作用をしていると思われる。

一方、NOは微生物や動物細胞で変異をおこす変異原性を示す。そこでNOによる発がん作用の可能性を検討するために、種々のNO発生剤を用いてマウス皮膚二段階発がん試験を行った。雌SENCARマウス（6週令）の背部皮膚にパーオキシナイトライト（PN）溶液を塗布し、TPAを続いて20週間、塗布を続けた。

試験終了時で腫瘍の発生率100%、腫瘍数は5から6個発生した。

この現象を遺伝子レベルで解析したところ、この腫瘍にH-rasコドン61番目に点突然変異を認め、この遺伝子の発現がPNによる腫瘍化に関連していると思われる。

この抑制実験として、クルクミン等の天然物由来化合物にPN誘発による腫瘍発生に対して抑制作用を示し、これらの化合物の有用性が示唆された。（天然物由来化合物の中にタベブイア・アベラネダエのデータを含んでいます。）

第74回 日本細菌学会総会

■2001年4月2日～4日　岡山県・岡山市

74nd General Meeting of the Japanese Society for Bacteriology

Rm031

「Anti-tumor activities of biologics」

生物製剤の抗腫瘍活性

Takusaburo Ebina
Division of Immunology, Miyagi Cancer Center Research Institute

われわれは副作用のない薬剤を求めて統合医学の推進をかかげた。西洋医学での薬剤は科学構造が明確な精製物であるが、量を間違えると毒物となり、常に副作用がつきまとう。一方漢方薬は数種類の生薬を混合したもので何が効いているかわからない欠点があり、他の薬との併用で副作用が問題となる。

そこで西洋医学でも漢方医学でもない第3の医学・統合医学を考案した。

統合医学での薬とは、構造や機能が明確な有効成分を含む抽出物を考えている。これはやっと機能性食品として認めはじめられたもので、すでに食品として受容されたものの抽出物なので、副作用がないのが特徴である。そこで今回は担子菌製剤、生薬、茶製剤についてその抗腫瘍効果を検討したので報告する。

担子菌カワラタケ抽出物PSKは蛋白質結合β-D-グルカンを主成分とする。担子菌アガリクス抽出物は蛋白結合α並びにβグルカンを主成分とする。一方担子菌シイタケ精製物レンチナンはβ-D-グルカンである。

マウス人工転移モデルにおいてPSK、アガリクス製剤は原発・転移両巣の増殖を抑えるのに対しレンチナンは全く抑えなかった。すなわち、抽出物の方が精製物より免疫能を増殖させて抗腫瘍効果を表すことがわかった。次にタマサキツヅラフジ抽出セファランチンと精製したアルカロイド剤を二重移植腫瘍系で比較すると、抽出セファランチンの方が抗腫瘍効果が優れていることがわかった。ノウゼンカズラ樹木抽出物タヒボ茶はナフトキノンを有効成分として含んでいる。タヒボ茶熱水抽出物を二重移植腫瘍系で調べると抗腫瘍効果があることがわかった。そこでPSK、アガリクス製剤、セファランチン、タヒボ茶の腫瘍細胞浸潤抑制能、腫瘍細胞に対するアポトーシス誘導能、血管内皮細胞に対する増殖抑制能を比較した。

■English translation

In our pursuit of integrative medicine, we aimed at finding drugs that cause no adverse drug reactions. Drugs used in Western medicine are purified subjects with identified chemical structures. However, these drugs can become a poison by a dosing error, and always accompany adverse drug reactions. On the other hand, the disadvantage of traditional Chinese prescriptions is that, since these prescriptions are the mixtures of several herbal medicines, the effective substance is unidentifiable. This is a problem in predicting adverse drug reaction in the concomitant use of a traditional Chinese prescription with other drugs. Therefore, "Integrative medicine" has been established as the third medicine, which is neither Western medicine nor Oriental medicine.
In integrative medicine, "drugs" are extracts containing active ingredients whose structures and functions have been identified. These "drugs" have just recently been recognized as functional foods and are extracts of the products that have already been approved as foods. Therefore, these "drugs" are characterized as having no adverse drug reactions. Under these circumstances, we investigated the anti-tumor effects of products from basidiomycete, a herbal medicine and a bark tea extract, and obtained the following results.
PSK, which is an extract from a basidiomycete species, kawaratake mushroom, contains β-D-glucan-protein complex as the major ingredient. The extract from another basidiomycete species, agaricus mushroom, contains α-D-glucan-protein complex and β-D-glucan-protein complex as the major ingredients. On the other hand, the major ingredient of lentinan, which is the purified substance from a basidiomycete species, shiitake mushroom, is β-D-glucan.
In an artificial metastasis model in mice, PSK and agaricus products inhibited the growth of both the primary and metastatic lesions, whereas no growth inhibition was observed with lentinan. In other words, it is demonstrated that extracts as compared with the purified substance exert a clear anti-tumor effect by enhancing immunocompetence. Then, cepharanthin extracted from Stephania cepharantha Hayata and the purified alkaloid were compared in the double grafted tumor system. As a result, the extracted cepharanthin had a higher anti-tumor effect. TAHEEBO tea, which is an extract from the bark of the NOUZENKAZURA tree, contains naphthoquinones as the major ingredient. The hot-water extract of TAHEEBO tea was examined in the double grafted tumor system and was found to have an anti-tumor effect. Therefore, PSK, agaricus products, cepharanthin, and TAHEEBO tea were comparable in their inhibition of tumor cell invasion, induction of apoptosis in tumor cells, and growth inhibition of vascular endothelial cells.