

The 7th Annual Meeting of Oncology Society of Japan

## 「Using the Medicinal Plant “Taheebo” in Integrated Cancer Medicine」

がん統合医療における薬用植物タヒボの使用経験

Shoji Hirata (Hirata Clinic for Oral and Maxillofacial Surgery and Medical Oncology, Cancer Care Village Sapporo)

近年がん治療において、現代西洋医学に自然治癒力を増強させることを目的に、サプリメントやいろいろな補完代替医療が併用される「がん統合医療」が注目されている。

なかでも、南米ブラジル・マゾン川流域に生育する薬用植物タバピア・アベラネダエ（通称：タヒボ）から分離・抽出された機能性成分「NQ801」は、癌や生活習慣病に対する有用性を示す数多くの研究結果が報告され、さらに正常細胞に対する安全性も確認されている。

「NQ801」は、タバピア・アベラネダエ（以降TAと記述）の樹皮（韌皮部）に含有される天然の植物色素ナフトキノンの一種で、とくに抗がん作用が注目されており、がん細胞に対する①直接作用（アポトーシス作用）と②間接作用（免疫賦活作用）、そして③補助作用（抗酸化作用、鎮痛・鎮静作用）が研究・報告されている。

そこで今回、当院で「NQ801」成分を含有するTAエキス末（樹皮を熱水抽出したエキスのスプレードライ加工品）を使用する機会を得たので、「NQ801」が「がん統合医療」にもたらす意義と役割について、臨床的な検討を行った。

方法は、がん統合医療を目的に①術前、②術後、そして③進行がん患者（緩和医療）に、TAエキス末と最近開発されたTA強化エキス末を飲用させ、その臨床効果を調べた。

TA強化エキス末は、TAエキスに「NQ801」フラクション分画を添加し、「NQ801」の含有量が6倍となるよう強化したエキス末品である。

その結果、TAエキス末（NQ801）を術前治療として低用量抗がん剤と固形がんに対し併用した場合、手術摘出組織の病理学的検索からNQ801は、DNAが損傷を受けたがん細胞周囲にCD4、CD8陽性T細胞を誘導・浸潤させることが示唆された（抗腫瘍効果：アポトーシス作用・免疫賦活作用）。また抗がん剤を使用している間も、副作用や食欲不振は見られなかった。

さらに術後に用いた場合、免疫増加や抗酸化作用による再発や転移予防の抑制も示唆され、再発予防としての使用意義も大きいと思われた。進行がん患者においても緩和医療やPalliative Therapyの一つとして、副作用を軽減しながら長期間の抗がん剤治療を可能にする役割も示唆された（腫瘍との共存）。また、今回使用した両エキス末を比べると、TA強化エキス末の方がより抗腫瘍効果が見られ、Dose dependence性も確認された。

以上より、有用成分「NQ801」の「がん統合医療」における使用意義は大きく、その役割も臨床研究が進めばさらに増えるものと思われる。今後各方面で同様の臨床研究が実施されることを期待したい。

### ■ English translation

In recent years, modern Western medicine is paying greater attention to “integrated cancer medicine”, which involves the concomitant use of supplements and various complementary and alternative medicines in cancer treatment, with an aim at reinforcing our natural healing abilities.

Many research results have particularly reported the utility against cancer and lifestyle-related diseases of “NQ801”, a functional element that is isolated and extracted from the medicinal *Tabebuia avellanedae* plant (commonly known as “Taheebo”) that grows in the Amazon River basin in Brazil, South America. Furthermore, its safety in regard to healthy cells has been confirmed.

NQ801 is a naphthoquinone natural colorant contained in the bark (the bast portion) of the *Tabebuia*

*avellanedae* (hereinafter referred to as “TA”), its anticarcinogenic effect is garnering special interest, and its 1) direct action (apoptotic effect), 2) indirect action (immunostimulatory effect) and 3) supplementary action (antioxidative, pain relieving and sedative effects) on cancer cells are being researched and reported on.

This hospital had an opportunity to use a TA extract powder (the spray-dried product of a hot-water extraction from TA bark) containing this NQ801 component, and carried out clinical examination on the significance and the role that NQ801 brings to “integrated cancer medicine”.

Pre-surgery, post-surgery, and advanced cancer (under palliative care) patients were given TA extract powder and a recently developed “Concentrated TA Extract Powder” to drink, and clinical efficacy was examined towards their application in “integrated cancer medicine”.

This Concentrated TA Extract Powder was the product of a TA extract fortified through the addition of NQ801-rich fractions, thus increasing the NQ801 content of by a factor of six.

The results from pathological retrieval of surgically-isolated tissue suggested that, when TA extract powder (NQ801) was used together with a low dosage anti-cancer drug as a pre-operative treatment against a solid carcinoma, NQ801 induced and permeated CD4- and CD8-positive T-cells in the area surrounding the cancer cell whose DNA was damaged (anti-tumoral effects: apoptotic and immunostimulatory activity). Moreover, neither side effects nor anorexia were observed during use of the anti-cancer drug.

Furthermore, prevention of recurrence and metastasis through increased immunity and an antioxidative effect was suggested when used post-operatively, and it is thought that there is a major significance in using NQ801 to prevent recurrence. Even for advanced cancer patients, a role for this extract was suggested in palliative care and palliative therapy due to its enabling long-term anti-cancer drug treatment (coexistence with tumors) while reducing side effects. In addition, when both extracts used in this study were compared, a higher anti-tumoral effect was observed with the Concentrated TA Extract Powder, and dose dependency was confirmed.

Thus, the significance of using a NQ801 component in “integrated cancer medicine” can be considered substantial and its role in this regard should increase greatly as clinical research advances. It is our hope that similar clinical research will be implemented in the future towards a variety of objectives.

The 7th Annual Meeting of Oncology Society of Japan

## 【Molecular biological evaluation of *Tabebuia avellanedae*, a medicinal plant with anti-tumoral efficacy – Particular comparison made to $\beta$ -Lapacho undergoing Phase II trials in the U.S.】

抗腫瘍効果を有する薬用植物タバブイア・アベラネダエの分子生物学的評価

—特に米国でphase IIにあるベータラパチョとの比較を交えて—

Harukuni Tokuda and Nobutaka Suzuki (Kanazawa University, Graduate School of Medical Science), Masafumi Kaneko and Mitsuaki Yamashita (Faculty of Pharmacy, Takasaki University of Health and Welfare), Bacowsky Helmut (Zentrum Nosomi Clinic), Akira Iida (Faculty of Agriculture, Kinki University)

治療の面から、ヒトにやさしい負担を軽減する思考より、加えて最近の補完代替医療の考え方を基に、南米産薬用植物で数世紀以前より種々の疾患に効果があるとされ、ヒトに対して連綿と使用されているブラジル産薬用植物、タバブイア・アベラネダエに関しての有用性を明らかにしている。

とくに現在の治療面での重要な項目である、がん発現に対するがん予防作用の効果、そのヒトへの応用に関しても、評価できるデータを得たので報告する。その基礎検討として、細胞を用いた試験と小動物を用いた試験を進めて、これまでのヒトでの作用に対する、裏付けの検証を目的に解析を行った。タバブイア・アベラネダエ(タヒボ)はるか数百年前より、とくに当時のインカ帝国で、その住民が様々な病態において使用続けた薬用植物であり、今だに繁用されている産物で、その意味からもヒトに対して、安全性の高い薬物と定義される。数十年前よりその内部樹皮から有用化合物が単離、構造決定され、詳細な研究が進められ、とくに含有するナフトキノ系化合物である、ベータラパチョは最近、アメリカ合衆国における薬剤開発の重要な試験で、がん治療を目的として、フェーズIIの終了段階まで進んでいる。

一方、今回の演者らも、同系化合物を独自に単離、構造解析を進めて、海外を含めた数カ国でその生物活性の特許を取得し、NQ801とした。

このように、米国の有力ベンチャー企業が同系化合物を開発している事実から、この素材のヒトでの有用性が確認されたとして、開発化合物であるベータラパチョとの比較も含めて、より詳細な生化学的、分子生物学的解析を通して、タヒボ並びにNQ801のヒトへの応用に向けての必要条件を見出したいと考えている。

### ■ English translation

Amongst the diversity of medicinal plants from South America, *Tabebuia avellanedae* (from Brazil) has been in continuous use by humankind for several centuries now as an especially effective treatment for various diseases. Its utility has been clarified from the aspect of therapy that considers reducing the burden on humans and is based on the concepts of present-day complementary and alternative medicine.

We will be reporting on the appreciable data that has been obtained regarding the effect of anticarcinogenic induction towards chemopreventive activity, an es-

pecially important item in cancer treatment today, as well as on the application of those measures to humans. As fundamental consideration in that regard, we conducted tests that utilize cells and tests that utilize small animals, and analyzed them for evidence supporting efficacy on humans to-date.

For many, many centuries, the medicinal *Tabebuia avellanedae* plant (commonly known as “Taheebo”) has been used by the local populace for various disease and conditions, especially during the ancient Inca Empire, and it is still in frequent use today. With that, it is defined as a medicine that is highly safe for human consumption. For several decades now, a useful compound from the internal bark of this plant has been isolated, its structure determined, and detailed research has been conducted. Recently, the  $\beta$ -Lapachone naphthoquinone compound that it contains has advanced to the final stages of Phase II testing in the United States in important studies related to pharmaceutical development in cancer treatment.

On the other hand, the presenters here have also independently isolated that same compound, conducted structural analysis, acquired patents for its biological activity in several countries worldwide, and named it “NQ801”.

With the utility of this substance on humans established through the development of that compound by powerful venture companies in the U.S., it is our goal to discover the necessary conditions of Taheebo and NQ801 in the application to humans through more detailed biochemical and molecular biological analyses and including a comparison with  $\beta$ -Lapachone, the compound currently under development.