6th Annual AACR International Conference

「Prevention of MAPK pathway by Brazilian medicinal plant, *Tabebuia avellanedae* on peroxynitrite induced carcinogenesis」

パーオキシナイトライト誘発ブラジル産薬用植物タベブイア・アベラネダエによるMAPK伝達系での抑制

Harukuni Tokuda (Department of Biochemistry, Kyoto Prefectural University of Medicine), Akira Iida (Faculty of Pharmacy, Takasaki University of Health and Welfare)

The present study was carried out to examine the chemo-preventive activity of natural Brazilian medicinal plant, *Tabebuia avellanedae* ext. and its components on peroxynitrite induced carcinogenesis. *Tabebuia avellanedae*, (TA) which is a plant that has been used for herbal medicine in South America and from Brazil to northern Argentina, is well known in traditional folk medicine used for the treatment of various disease during five hundred years. The inner bark of this plant produced in Brazil is distributed in Asia as a herb tea and healthy purpose. On the fundamental findings, several studies have suggested that these compounds, anti-oxidatives were observed the inhibitory effect against chemical carcinogenesis induced tumor initiating and promoting activity using two-stage mouse skin model. In the course of these studies, female SENCAR mouse (6 weeks of age) were treated topically with single dose of PN solution, followed by TPA twice a weekly for 20 weeks. Tumor incidence were 100% with 6 to 7 per mouse at end of experiment as positive control group. TA powder were orally fed with drinking water for only 2 weeks, before and after initiation and following promoting treatment with drinking water only, as test compounds. In our observation, TA and its components treated group cause about 60-70% reduction in the average number of tumors per mouse after 20 weeks of experiment, respectively. Topical administration of TA and its components had much influence against PN induced expression stage. We postulate that these data suggest possible role of a regulatory mechanism of chemopreventive activity in PN induced carcinogenesis. Employing Western blot analysis studies, we found that H-Ras, MEK-2 and p38 levels observed the effects against PN induced activation, and more detail Western blot analysis indicated a active decrease in p38 expression in the skin after TA treatment. Summary of our findings, we suggest that one target of TA and its component effects in mouse skin is the modulation or regulation of the MAPK signaling.

■日本語要約

この研究は、パオキシナイトライト(PN)で誘発される発がんにおけるブラジル産薬用植物に関して、がん予防活性について試験をおこなった。タベブイア・アベラネダエ（TA）は、南米のブラジルから北部アルゼンチンにかけて自生する樹木で、薬用植物として、500年以上に亘って種々の疾患に対して伝承薬物として使用されてきた。ブラジル産であるこの樹木の内部樹皮は、アジアでは主に飲料茶として供給されている。基礎的な知見として、我々の実験より抗酸化活性を含むこれら化合物が、マウス皮膚二段階発がん試験を用いて発がんイニシエーションとプロモーションにおいて抑制効果を示した、これらの研究として、雌SENCARマウス（6週令）をPNにて単回処理した後、さらに20週間TPA塗布を続けた。腫瘍発生率・腫瘍個数は、無処理の場合、実験終了時に100%と6〜7個を示し、TAエッセンスまたはそこに含まれるNQ801をイニシエーション前後2週間のみ処理すると、それぞれ60〜70%の抑制を示した。このことから、TAまたはその素材は、PNによる発がん誘発段階に影響をおよぼすことが判明した。このデータのさらに詳細な検討として、ウエスタンブロット法を用いて解析した結果、H-Ras、MEK、P38段階での作用が認められ、とくにTA処理の皮膚ではP38の発現が減少した。この知見の要約として、われわれはTAエッセンスとその素材のひとつの標的として、マウス皮膚ではMAPK伝達の調整をおこなっていることが示唆された。