

The examination is being carried out on the **following application documents**

Description, Pages

1-31 as published

Claims, Numbers

1-9 as published

Drawings, Sheets

1/13-13/13 as published

- 1 The present application relates to a composition for preventing/treating cancer, said composition containing as an active ingredient a Taxus cambium or procambium derived cell line, a lysate or an extract thereof. The problem to be solved resides in the provision of a natural material-derived anticancer composition with minimized side effects compared to the conventional anticancer agents. The solution offered in the present application comprises cambium- or procambium-derived cell lines overcoming the problem of variation caused by dedifferentiation and which proliferate stably whereby the anticancer effect of the present cell lines does not rely on the action of paclitaxel.
- 2 Reference is made to the following documents; the numbering will be adhered to in the rest of the procedure.
 - D1 ZOCHER R ET AL: "Biosynthesis of taxol: enzymatic acetylation of 10-deacetylbaecatin-III to baecatin-III in crude extracts from roots of Taxus baccata.",
BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS 4
DEC 1996 LNKD- PUBMED:8954077,
vol. 229, no. 1, 4 December 1996 (1996-12-04), pages 16-20,
XP002325536,
ISSN: 0006-291X
 - D2 HEZARI M ET AL: "Purification and characterization of taxa-4(5),11(12)-diene synthase from Pacific yew (Taxus brevifolia) that catalyzes the first committed step of taxol biosynthesis.",
ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS 1 OCT 1995 LNKD-
PUBMED:7574719,

vol. 322, no. 2, 1 October 1995 (1995-10-01), pages 437-444,
XP002945172,
ISSN: 0003-9861

D3 STROBEL G A ET AL: "Taxol formation in yew - Taxus",
PLANT SCIENCE, ELSEVIER IRELAND LTD, IE,
vol. 92, no. 1, 1 January 1993 (1993-01-01), pages 1-12, XP023484303,
ISSN: 0168-9452, DOI: DOI:10.1016/0168-9452(93)90060-D
[retrieved on 1993-01-01]

D4 RUSSIN WILLIAM A ET AL: "Immunocytochemical localization of taxol in
Taxus cuspidata",
INTERNATIONAL JOURNAL OF PLANT SCIENCES,
vol. 156, no. 5, 1995, pages 668-678, XP009146461,
ISSN: 1058-5893

D1 reports on the biosynthesis of taxol as a multistep process focusing on the acetylation of 10-deacetylbaccatin-III (10-DAB) to yield baccatin-III as precursor of taxol in an intermediate reaction, whereby crude extracts from cambium of stems yield a three- to fivefold lower activity (cf. abstract, and introduction on front page 16, page 17, last para. to page 19, 3rd para.). However, although being devoid of paclitaxel, D1 apparently does not explicitly disclose an anti-cancerous effects of the precursors of taxol.

D2 focuses on the purification and characterization of taxa-4(5),11(12)-diene synthase from Taxus brevifolia catalyzing the committed step of taxol biosynthesis (cf. summary). On page 438, left-sided col., D2 reports about very low levels of taxadiene synthase activity in yew stem cells and about trace amounts of of taxadiene intermediate in the bark. On page 440, 2nd para. of the left col., D2 reports that dissection of yew stems and comparison of the corresponding extracts with those of other yew tissues demonstrate that the taxadiene synthase activity resides almost exclusively in the peeled bark and adhering cambium cells with little activity associated with the xylem and wood stem core. It can be concluded therefrom that the presence of **taxol intermediates** is rather confined to the bark and the adhering **cambium** cells in contrast to the presence of taxol in the woody stem core, needles and roots.

D3 relates to the formation of taxol in yew (Taxus) which is found most abundantly in the **vascular cambial** region followed by the phloem, sapwood and heartwood. Being known that only traces of taxol biosynthesis are demonstrated in the xylem, it appears that taxol is mobilized from its place of greatest biosynthetic activity (the vascular cambial region) to to xylem (cf.

abstract). However, the most important source of taxol resides in the bark (phloem and cambium) of the mature yew (cf. page 1, right col., page 5, last para. of the left col. bridging with line 7 of the right-hand col.). D3 apparently tries to elucidate the taxol biosynthesis in various tissues and its mobilization in the yew tree.

D4 studies the localization of taxol in *Taxus cuspidata* by immunocytochemical methods using polyclonal antitaxol antiserum on cryopreserved tissues showing that taxol is accumulated in the **cell walls** of bark, wood and leaves (cf. abstract and 2nd para. on the right col. of page 676).

Compositions comprising taxol isolated from the bark (phloem/cambium) of the *Taxus* species of the mature yew are known in the prior art. However, due to the taxol biosynthesis in various tissues of the *Taxus* species and to the mobilization of taxol and taxol **intermediate** compounds throughout the tree, the fractions obtained and referred to in the cited documents apparently belong to cell lines derived from the cambium/procambium of **Taxus** and do not exert their action due to the presence of paclitaxel. Although the cited documents do not explicitly disclose or suggest the use of the mentioned taxol intermediates in the wide-spread field of anti-cancer therapy, the skilled practitioner, would be tempted to try further compounds with a closely related chemical structure in the same technical field with reasonable expectation to succeed. So far, the present subject-matter does not appear to distinguish in a non-obvious and inventive manner over the prior art knowledge pursuant to the requirements of Art. 56 EPC.

Moreover, the obtention of cell lines using an isolation method comprising the step of obtaining a *Taxus* cambium- or procambium-containing tissue and culturing/collecting said cell line appears to form part of the common prior art and not novel nor inventive.

- 3 A third partie's observation letter under Art. 115 EPC has been filed with letter of 24/09/2010 disputing novelty and inventive step of the present application with reference to the application EP2227247 allegedly anticipating the teaching of the present application. The Examining Division considers the teaching of this document identical to that of the present application and expects the Applicant to raise his comments hereto.
- 4 Claim 1 is characterized by a "cell line derived from the cambium or procambium of *Taxus*": However, the non-limiting terms "large number of vacuoles", "innately undifferentiated state" and "it is a homogenous cell line" in claim 1 do not provide any distinguishing information as to the structure or nature of the intended cells. Said unclear definitions hence put an undue

burden on the skilled person seeking to establish the scope of the claims and willing to carry out the invention over the whole of the broad field claimed (Arts. 83 and 84 EPC).

This also applies to the characterizing features (a) to (c) which have to be construed as the mere attempt to define the invention by the result to be achieved (cf. in the Guidelines, C-III, 4.10).

- 5 Claims 5-9 cover a method of treatment of the animal or human body, which is not regarded as susceptible of industrial application within the terms of Art. 53 (c) EPC. In this context it has to be noted that passages throughout the description referring to a method of treatment are to be removed or so redrafted as to indicate a possible application of the invention.
- 6 The application contains general statements in the description trying to extend the scope of protection in an ambiguous way (cf. page 31, last para.). See hereto in the Guidelines of the EPC, C-III, 4.4.