

Internal distribution code:

- (A) Publication in OJ
(B) To Chairmen and Members
(C) To Chairmen
(D) No distribution

**Datasheet for the decision
of 18 May 2009**

Case Number: T 0492/08 - 3.3.08

Application Number: 00938999.0

Publication Number: 1257649

IPC: C12N 15/31

Language of the proceedings: EN

Title of invention:

Corynebacterium glutamicum genes encoding metabolic pathway proteins

Applicant:

Paik Kwang Industrial Co., Ltd.

Headword:

Corynebacterium/PAIK KWANG

Relevant legal provisions:

EPC Art. 56

Relevant legal provisions (EPC 1973):

-

Keyword:

"Inventive step (yes)"

Decisions cited:

-

Catchword:

-



Case Number: T 0492/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 18 May 2009

Appellant: Paik Kwang Industrial Co., Ltd.
31 Soryong-dong, Gunsan-si
Jeollabuk-do (KR)

Representative: Maiwald Patentanwalts GmbH
Elisenhof
Elisenstrasse 3
D-80335 München (DE)

Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 8 October 2007
refusing European application No. 00938999.0
pursuant to Article 97(1) EPC 1973.

Composition of the Board:

Chairman: L. Galligani
Members: T. J. H. Mennessier
C. Rennie-Smith

Summary of Facts and Submissions

- I. The applicant (appellant) lodged an appeal against the decision of the examining division dated 8 October 2007, whereby the European patent application No. 00 938 999.0 with publication number 1 257 649 was refused. The application, entitled "*Corynebacterium glutamicum* Genes Encoding Metabolic Pathway Proteins", originated from an international application published as WO 01/00843.
- II. The decision was based on the request filed with the letter of 13 June 2007 (claims 1 to 32) which was refused for reasons of lack of inventive step (Article 56 EPC) in view of document D2 which was considered to represent the closest state of the art taken together with document D1 (see Section VII *infra*). The decision contained additional remarks on the non-compliance of the invention with other requirements of the EPC.
- III. On 18 February 2008, the appellant filed a statement setting out the grounds of appeal which was accompanied by a new request (claims 1 to 12) to replace the request refused by the examining division. The appellant requested that the decision under appeal be set aside and a patent be granted on the basis of that request. As an auxiliary measure, oral proceedings were requested.
- IV. The examining division did not rectify its decision and referred the appeal to the board of appeal (Article 109 EPC).

V. In a phone call on 12 February 2009, the appellant was informed that the board was inclined to consider favourably the request filed with the statement of grounds provided that a clarity problem affecting claims 8 and 10 then on file was solved.

VI. In reply to the board's phone call, the appellant filed on 7 April 2009 a new request (claims 1 to 10). That request was intended to replace the previous claim request from which it differed in that claim 8 had been amended and claims 10 and 11 had been deleted, with previous claim 12, now claim 10, having been corrected to remove two typing errors (the latin species names "*acetuphilum*" and "*paraffinolytcum*" have been amended to "*acetophilum*" and "*paraffinolyticum*", respectively).

Claims 1, 2 and 3 read as follows:

"1. An isolated *Corynebacterium glutamicum* nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:1, or a nucleic acid sequence, which is at least 90% identical to SEQ ID NO:1."

"2. An isolated nucleic acid molecule which encodes a polypeptide sequence comprising the amino acid sequence set forth in SEQ ID NO:2, or a protein, which is at least 90% identical to SEQ ID NO:2."

"3. A vector comprising the nucleic acid molecule of any one of claims 1 or 2."

Claim 4 was dependent on claim 3 and directed to a particular embodiment thereof.

Claim 5 read as follows:

"5. A host cell transfected with the expression vector of claim 4."

Claims 6 and 7 were dependent on claim 5 and each directed to a particular embodiment thereof.

Claim 8 read as follows:

"8. A method for producing lysine, comprising culturing the cell of claim 7 such that lysine is produced."

Claims 9 and 10 were dependent on claim 8 and each directed to a particular embodiment thereof.

VII. The following documents are referred to in the present decision:

(D1) Database EMBL Sequences [online], Accession number 033231, 15 December 1998

(D2) B. J. Eikmanns et al., Antonie van Leeuwenhoek, Vol. 64, No. 2, June 1993, Pages 145 to 163

(D3) S. T. Cole et al., Nature, Vol. 393, 11 June 1998, Pages 537 to 544

(D4) B. Bathe et al., Mol. Gen. Genet., Vol. 252, 1996, Pages 255 to 265

VIII. The submissions made by the appellant, insofar as they are relevant to the present decision, may be summarised as follows:

Article 56 EPC

Starting from document D2 taken as the closest state of the art, the technical problem to be solved might be regarded as the selection of one of ten different genes from two different synthesis pathways in order to provide an improved process for producing lysin. The skilled person was therefore facing the problem of selecting the *dapF* gene encoding the diaminopimelate epimerase from two synthesis pathways and ten genes. Document D3 (referred to as document D1 in the statement of grounds) disclosed a linear map of the chromosome of *Mycobacterium tuberculosis* H37Rv showing the position and orientation of 3,924 known genes including a *dapF* gene encoding a diaminopimelate epimerase, the amino acid sequence of which was given in document D1. That sequence had 61% homology with the sequence of the diaminopimelate epimerase of the application (see SEQ ID NO:2). The skilled person would have found no guidance in document D3 pointing to the advantages associated with the use of diaminopimelate epimerase for the synthesis of lysine. The choice of the *dapF* gene of *Corynebacterium glutamicum* could not have been made without hindsight.

- IX. The appellant requests that the decision under appeal be set aside and a patent be granted on the basis of claims 1 to 10 filed on 7 April 2009.

Reasons for the Decision

Requirements of Article 123(2) EPC (prohibition of added matter)

1. Support is found in application WO 01/00843, which is the published version of the application as filed:
 - 1.1 As regards claim 1 (nucleic acid molecule): on page 6 (lines 15 to 25).
 - 1.2 As regards claim 2 (nucleic acid molecule): on page 6 (lines 25 to 28) in combination with pages 26 (lines 22 to 27), 27 (lines 11 to 15) and 31 (lines 16 to 17).
 - 1.3 As regards claims 3 to 7 (vector and host cell): in addition to the afore-mentioned pages, on page 8 (lines 1 to 3, 6 to 7 and 18 to 20) in combination with page 41 (lines 4 to 6 and 12 to 17).
 - 1.4 As regards claims 8 to 10 (method for producing lysine): in addition to the afore-mentioned pages, on page 8 (lines 21 to 22) in combination with pages 10 (lines 15 to 20) and 91 to 94 (Table 3) as well as claim 29.
2. In conclusion, there are no objections under Article 123(2) EPC to the amendments introduced in the claims.

Requirements of Article 56 EPC (inventive step)

3. Claim 1 is directed to the DNA sequence, as represented in SEQ ID NO:1, encoding the diaminopimelate epimerase of the ATCC 13032 strain of *Corynebacterium glutamicum*

- while claim 2 is directed to the amino acid sequence of that enzyme, as represented in SEQ ID NO:2.
4. Document D2 is considered to represent the closest state of the art. Reminding the reader that *Corynebacterium glutamicum* is used for the industrial production of L-lysine (see abstract, first sentence), the document states that it has been established since 1991 that in *Corynebacterium glutamicum* the biosynthesis pathway from L-piperideine-2,6-dicarboxylate to L-lysine is split into two parallel routes (see Figure 1 on page 147), namely the diaminopimelate dehydrogenase (encoded by the *ddh* gene) route with a single enzymatic reaction and the succinylase route with a series of four enzymatic reactions involving the enzymes encoded by the *dapD*, *dapC*, and *dapE*, and lastly the diaminopimelate epimerase (encoded by the *dapF* gene) in that order. Both routes are found in both the wild type strain and in several lysine-producing strains (see page 152, left-hand column). Only the diaminopimelate dehydrogenase route of the pathway from L-aspartate to L-lysine is described with detailed information as to the organisation and structure of genes and their regulation (see pages 149 to 151).
 5. In view of document D2, the technical problem to be solved may be seen as the effective provision of the nucleic acid molecule encoding a polypeptide having diaminopimelate epimerase activity derived from *Corynebacterium glutamicum* and useful for the industrial production of lysine. The solution to that problem is a nucleic molecule according to claim 1 (see SEQ ID NO:1) encoding a polypeptide according to

- claim 2 which is the diaminopimelate epimerase of the ATCC 13032 strain of *Corynebacterium glutamicum* (see SEQ ID NO:2).
6. For the assessment of inventive step, the question to be answered is whether the skilled person, using document D2 as starting point, would have found an incentive in the state of the art to choose the known ATCC 13032 strain, to clone and sequence the relevant gene and to test the encoded diaminopimelate epimerase for its usefulness in the industrial production of lysine.

 7. Document D1 which has been relied on by the examining division cannot be regarded as relevant. The reason therefor is that the document discloses the amino acid of a polypeptide having diaminopimelate epimerase activity isolated from a bacterial strain of *Mycobacterium tuberculosis* which has found extensive application in biomedical research (see e.g. document D3, page 537, right-hand column, second full paragraph), whereas the skilled person is looking for a *Corynebacterium glutamicum* species known to be useful in the field of the industrial production of lysine. The skilled person would have simply ignored document D1. Moreover, technically speaking, the contention of the examining division that document D1 would have provided the skilled person with the means to embark on the cloning of the *dapF* gene of the invention is not tenable. Indeed, document D1 does not contain information about any nucleic acid sequence from which primers could be derived and used in an amplification process. Rather, it contains information about an amino acid sequence which, in any case, as noted by the

appellant in its statement of grounds, differs significantly from SEQ ID NO:2.

8. The skilled person would have rather considered document D4 for the reason that it discloses a physical and genetic map chromosome of the known ATCC 13032 prototype strain of *Corynebacterium glutamicum*. Table 3 (see page 361) reports the localisation of a number of gene probes, including probes for the *dapD*, *dapC* and *dapE* genes, encoding three of the four enzymes involved in the succinylase route of the biosynthesis pathway from aspartate to L-lysine (see document D2, Figure 1, page 147) but does not include a probe for the *dapF* gene. As document D4 as a whole is silent as regards that particular gene, the skilled person would not have found therein the necessary guidance to improve the resolution of the available map, find its precise localisation, clone and sequence it without initiating a research program.

9. Therefore, the board is of the view that the skilled person would have not found any incentive in the state of the art to arrive at the invention. Thus, claims 1 and 2 involve an inventive step, the same conclusion applying *de facto* to the remaining claims, the subject-matter of which is defined with a back-reference to claim 1 or claim 2.

Other requirements of the EPC

10. The decision under appeal (see Section IV on pages 4 to 6) also pointed to further defects affecting some of the claims then on file, which therefore might have been objected to under Articles 54, 56, 83 and 84 EPC.

As those claims have been either deleted or suitably amended, there is no need to consider further those additional remarks of the examining division.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the examining division with the order to grant a patent on the basis of claims 1 to 10 filed on 7 April 2009 together with a description to be adapted thereto.

The Registrar

The Chairman

A. Wolinski

L. Galligani