The opinion in support of the decision being entered today was not written
for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte STEPHEN J. BENKOVIC, MARC OSTERMEIER,
STEFAN LUTZ and ANDREW E. NIXON

Appeal No. 2005-1912
Application No. 09/718,465

ON BRIEF

Before ADAMS, MILLS, and GREEN, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 5, 6, 9, 38 and 39, which are all of the claims pending in this application.

Claim 5 is representative of the claims before us and is set forth below:

5. A method of making a plurality of incrementally truncated hybrid nucleic acids comprising the steps of:

a) providing a first and second parent nucleic acid;

b) serially removing nucleotides from one or both termini of said first and second parent nucleic acid to form truncated first and second parent nucleic acids whose length decreases incrementally over time;

c) stopping said serially removing nucleotides at a plurality of different times to form a plurality of incrementally truncated first and second parent nucleic acids; and

d) linking separate incrementally truncated first parent nucleic acids to separate incrementally truncated second parent nucleic acids to form a plurality of incrementally truncated hybrid nucleic acids.

The prior art reference relied upon by the examiner is:

Ostermeier et al. (Ostermeier), "Combinatorial Protein Engineering by Incremental Truncation," Proc. Natl. Acad. Sci. USA, Vol. 96, pp. 3562-3567 (1999).

Grounds of Rejection

Claims 5-6, 9, 38-39 are rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

Claims 5-6, 9, 38-39 are rejected under 35 U.S.C. § 102(a) for anticipation over Ostermeier.

We affirm the rejection for anticipation and do not reach the rejection for lack of enablement.

Claim Grouping

According to appellants, the rejected claims 5-6, 9, and 38-39 stand or fall together. Brief, page 5. Therefore, we select claim 5 as representative of the claims on appeal. 37 CFR § 1.192(c)(7), now 37 CFR ' 41.37(c)(1)(vii) (2004).

DISCUSSION

Claims 5-6, 9, 38-39 are rejected under 35 U.S.C. § 102(a) for anticipation over Ostermeier.

According to the Examiner, (Answer, page 6):

> Ostermeier [ ] teach combinatorial protein engineering by incremental truncation. The reference discloses a combinatorial approach using incremental truncation libraries of overlapping N- and C-terminal gene fragments are developed. The reference discloses Libraries of all possible combinations of length of N-terminal and C-terminal protein fragments are constructed (i.e., see page 3562, right column). Figure 1, in page 3563 depicts the invention. The reference discloses that the purN gene was divided into N-terminus fragment and C-terminus fragment (refers to the parent nucleic acids of the instant claims). The reference uses Exo III digestion to remove incremental nucleic acids from the purN gene fragments (refers to step b of the instant claims). The resulted incremental truncation fragments (or libraries) are cloned into an auxotrophic E. coli strain (refers to instant claim 6). The reference teaches PurN gene sequence was fragmented into a plurality of fragments (refers to the instant claim 9). Thus the reference clearly anticipates the claimed invention.

We agree for the reasons set forth in the Examiner's Answer that the examiner has established a prima facie case of anticipation based on the evidence before us. Ostermeier describes each of the claimed method steps and evidences the preparation of a plurality of hybrid nucleic acids, e.g., hybrid nucleic acids from genes A and B which have been subjected to truncation prior to hybridization with one another (recombination) using the incremental truncation method. See Ostermeier, page 3563, column 1; Fig. 1. While we recognize that the primary objective of Ostermeier was to determine which physically separate fragments of an enzyme can physically associate

to form heterodimers which restore enzyme function (Ostermeier, page 3562, abstract; Brief, page 24), we also recognize, as did the examiner, that Ostermeier describes that some hybrid nucleic acids formed by recombination. Ostermeier, page 3564, column 2.

"[A]fter the [examiner] establishes a prima facie case of anticipation … the burden shifts to appellant to 'prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.'" In re King, 801 F.2d 1324, 1327, 231 USPQ 136, 138 (Fed. Cir. 1986) (quoting In re Swinehart, 439 F.2d 210, 212-13, 169 USPQ 226, 229 (CCPA 1971)).

In rebuttal, appellants assert that Ostermeier does not teach step (d) of claim 5. Brief, page 26. Appellants argue that (Brief, pages 24-25)

> Linking, according to step d), is an event whereby hybrid incrementally truncated nucleic acids are formed from first and second incrementally truncated parental nucleic acids. This step is described on page 25 of the Application (line 1) and "can include the step of fusing and/or ligating" parental nucleic acids, and a diagram of one type of linking is shown in Figure 3. Incrementally truncated parental nucleic acids can be indirectly joined such that the resulting hybrid incorporates additional nucleotides not present in either parent or directly joined, giving "seamed" and "seamless" hybrid nucleic acids, respectively (Application page 31, line 26 and page 32, line 11.
>
> Ostermeier et al., (1999) teaches, by contrast, a system for determining which, if any, physically separate fragments of an enzyme can physically associate to restore enzyme function. Their methodology was to co-infect cells with physically separate N-terminal and C-terminal enzyme nucleic acid fragments. Where enzyme function was subsequently found, the enzyme fragments encoded by these N- and C-terminal gene fragments were concluded to have been able to interact so as to restore enzyme function. . . . Recombinants were very rare, comprising less that 0.04% of co-infectants (fewer that 1 in 2,500). . . .
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> No linking of the incrementally truncated parental nucleic acids to form a hybrid nucleic acid is taught by Ostermeier, nor is linking an inevitable and certain result of Ostermeier's experimental procedure as is required by the law for inherency to be found.

Brief, paragraph bridging pages 25-26.

The examiner responds, arguing "Ostermeier et al teach recombination is found to occur, and [teach] recombinants containing intact purN gene, apparently resulting from recombination between the two plasmids. Thus, the reference teaches 'linking separate incrementally truncated first and second parent nucleic acids.'" Answer, page 12. We agree with the examiner, and are not persuaded by appellants' arguments.

In particular, with respect to appellants' argument that the concept of "linking" in step (d) includes or is limited to fusing or ligating nucleic acids, the examiner acknowledges that these features are <u>not</u> "recited in the rejected claim(s)" and thus cannot distinguish the invention claimed from Ostermeier. Answer, page 13. We again agree with the Examiner's claim interpretation. It is well settled that during <u>ex parte</u> prosecution, claims are to be given their broadest reasonable interpretation consistent with the description of the invention in the specification. <u>In re Zletz</u>, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). Thus, we interpret the term "linking" in the claim, in its broadest sense, to mean "joining". Even appellants' own characterization of the concept of linking in the specification and the Brief, as "direct or indirect or seemed or seamless" is consistent with the broad concept of "joining". Furthermore, the specification, pages 8-9, describes that "isolated nucleic acid inserts are **recombined** for a time period and under conditions suitable to form a plurality of

shuffled incrementally truncated nucleic acids" and "the recombining comprises mixing the isolated nucleic acid inserts . . . to form a mixture of nucleic acid fragments" and joining the nucleic acid fragments of the mixture with a ligating enzyme. [Emphasis added.] Therefore, the specification contemplates joining truncated nucleic acids through recombination, as described by Ostemeier.

Furthermore, Ostermeier describes that hybrids of gene library A and gene library B were isolated and transformed into auxotroph E. coli requiring GAR transformylase for growth, to confirm that complementation only resulted when both plasmids were present. Ostermeier, page 3564, column 2. "Recombination was found to occur, ostensibly because the auxotroph is recA+ and because of the large overlap of homogeneous sequences (up to 243) if a cell happens to receive a long N-terminal and C-terminal purN gene fragment." Id. Thus, Ostermeier clearly teaches that the resulting intact purN gene encoding GAR transformylase is due to the recombination[1] (joining) of the separate gene plasmids, which are composed of incrementally truncated parent nucleic acids from two separate libraries. See Figure 1 of Ostermeier. Answer, page 13.

1 Note the gene fragments chosen for the libraries have up to 243 bp of overlap. Ostermeier, page 3564, column 2. Thus fusions between the two genes occurred in the region of overlap. Further attention is directed to Ostermeier et al. (Ostermeier 2), "A combinatorial approach to hybrid enzymes independent of DNA homology," Nature Biotechnology, pp. 1205-1209 (1999). [Of record 11-06-2003]. Ostermeier 2 contains disclosure similar to that of Ostermeier and further confirms that recombination in regions of overlap is due to covalent fusion of the gene fragments in the region of overlap. Ostermeier 2, page 1206.

Appellants further argue that the “rare and unpredictable co-infected gene fragment recombination events postulated by Ostermeier cannot be natural, inevitable and necessary result of Ostermeier's disclosure as required by Federal Circuit inherency jurisprudence.” Brief, page 26. The examiner found these assertions of appellants to be unpersuasive because the rejection of record is not based on inherency, and that “the reference clearly teaches that complementation (presence of intact purN gene) only resulted when both plasmids were present.” Answer, page 13. We agree with the examiner, for the reasons herein, that Ostermeier anticipates the claimed method directly, without reliance on principles of inherency.

In view of the above, we do not find appellants have presented convincing argument to rebut the examiner’s prima facie case of anticipation. The rejection of the claims for anticipation is affirmed.

CONCLUSION

The rejection of claims 5-6, 9, 38-39, under 35 U.S.C. § 102(a) for anticipation over Ostermeier is affirmed. We do not reach the merits of the rejection of the claims for lack of enablement as all claims have been disposed of by the anticipation rejection.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR ' 1.136(a).

AFFIRMED

DONALD E. ADAMS Administrative Patent Judge	)
DEMETRA J. MILLS Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
LORA M. GREEN Administrative Patent Judge	)

DJM/lbg

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