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Datasheet for the decision
of 27 September 2006

Case Number: T 1171/01 - 3.5.01

Application Number: 97919229.1

Publication Number: 0901665

IPC: G06K 9/00, G01N 15/14

Language of the proceedings: EN

Title of invention:
Method and apparatus for automatically detecting malignancy-
associated changes

Applicant:
MonoGen, Inc.

Opponent:
-

Headword:
Detecting malignancy-associated changes/MONOGEN

Relevant legal provisions:
EPC Art. 54, 56, 123(2)

Keyword:
"Inventive step (no)"

Decisions cited:
T 1173/97

Catchword:
-

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Case Number: T 1171/01 **-** 3.5.01

D E C I S I O N
of the Technical Board of Appeal 3.5.01
of 27 September 2006

Appellant: MonoGen, Inc.
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Representative: Spall, Christopher John
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Decision under appeal: **Decision of the Examining Division of the**
                                  European Patent Office posted 30 March 2001
                                  refusing European application No. 97919229.1
                                  pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: S. Steinbrener
Members: R. Wibergh
                   P. Schmitz

Summary of Facts and Submissions

I.   This appeal is against the decision of the examining
        division to refuse European patent application
        No. 97 919 229.1.

II.   The following documents will be referred to in the
        present decision:

        D1: EP-A-0 595 506
        D2: WO-A-96/09605.

III.   According to the decision appealed document D1,
        regarded as disclosing the closest prior art,
        anticipated the invention as defined in claim 1 in the
        version of 21 February 2001 or at least rendered it
        obvious in combination with D2.

IV.   Claim 1 read (including two corrections requested by
        the appellant by letter dated 25 August 2006):

        "A method of detecting malignancy-associated changes in
        a cell sample, comprising the steps of:
        obtaining a cell sample;
        staining the sample to identify cell nuclei within the
        sample;
        obtaining an image of the cell sample with a digital
        microscope of the type that includes a digital CCD
        camera and a programmable slide stage;
        recording the image in a computer system;
        focusing the image;
        identifying objects in the image;
        calculating a set of feature values for each object;
        and

analyzing the feature values to determine whether each
object is a cell nucleus; and computing a set of
feature values for each nucleus found in the sample and
from the feature values determining whether the nucleus
exhibits malignancy-associated change, and
characterised in that
the determination is made by a classifier constructed
from a first database comprising feature values
obtained from apparently normal cells of a healthy
patient and a second database comprising feature values
obtained from apparently normal cells of an abnormal
patient".

V.   With the statement of grounds of appeal dated 23 July
        2001 the appellant requested that the decision be set
        aside and a patent be granted based on claim 1 on file
        or on one of three alternative claims filed together
        with the grounds of appeal.

VI.   Alternative claim 1 differed from the main request in
        that it was directed to a method of detecting
        malignancy-associated changes in a cell sample "for
        further investigation" and that it contained the
        further steps of

        "determining a ratio of nuclei determined to exhibit
        malignancy-associated changes to the total nuclei in
        the subsample;
        comparing the ratio to a predetermined threshold; and
        determining the need for further investigation if the
        ratio exceeds the predetermined threshold".

VII.   Alternative claim 2 mainly differed from alternative
        claim 1 in that there was no mention of first and
        second databases.

VIII.   Alternative claim 3 differed from alternative claim 2
        in that it was directed to a "method of detecting
        malignancy-associated changes in a cell sample of a
        patient to determine the need for further investigation
        of changes suggestive of cancer in the patient".

IX.   By communication dated 6 August 2004, the Board
        observed in respect of the alternative claims that
        there appeared to be no original support for the
        feature "determining the need for further investigation
        if the ratio exceeds the predetermined threshold".
        Reference was made to the different statement at
        page 13, lines 6 to 9 of the application.

X.   By letter dated 25 August 2006 in response to a summons
        to oral proceedings, the appellant requested two minor
        corrections to claim 1 of the main request (cf.
        point IV *supra*) and filed two further claim versions:
        "Claim A" and "Claim B".

XI.   Claim A differed from claim 1 according to the main
        request in that "cancer patient" replaced "abnormal
        patient" (cf. the final feature of the claim).

XII.   Claim B read:

        "A classifier for detecting the presence of malignancy
        associated changes (MAC) in a cell nucleus, wherein the
        classifier is constructed using a first database
        comprising feature values obtained from apparently
        normal cells which were known to come from healthy

patients and a second database comprising feature values obtained from apparently normal cells which were known to come from cancer patients, wherein data from said databases is used to develop a discriminant function that can discriminate between MAC-positive nuclei and MAC-negative nuclei".

XIII.   Grant of a patent was requested in accordance with a main request and ten auxiliary requests. These requests were based on the following independent claims:

Main request:
Claim 1 of 21 February 2001 (including the corrections filed on 25 August 2006) and claim B as claim 11;

Auxiliary request 1:
Claim 1 of 21 February 2001 (including the corrections filed on 25 August 2006);

Auxiliary request 2:
"Alternative claim 1" of 23 July 2001 as claim 1, and claim B as claim 11;

Auxiliary request 3:
"Alternative claim 2" of 23 July 2001 as claim 1, and claim B as claim 11;

Auxiliary request 4:
"Alternative claim 3" of 23 July 2001 as claim 1, and claim B as claim 11;

Auxiliary request 5:
"Alternative claim 1" of 23 July 2001 as claim 1;

Auxiliary request 6:

"Alternative claim 2" of 23 July 2001 as claim 1;

Auxiliary request 7:

"Alternative claim 3" of 23 July 2001 as claim 1;

Auxiliary request 8:

Claim A as claim 1 and claim B as claim 11;

Auxiliary request 9:

Claim A as claim 1;

Auxiliary request 10:

Claim B as only claim.

XIV.   Oral proceedings, which the appellant did not attend,
       were held on 27 September 2006. After deliberation the
       Board announced its decision.

Reasons for the Decision

1.   Background of the invention

       The invention is a method of detecting malignancy-
       associated changes (MACs) in a cell sample. As
       explained in the application, MACs are "subtle changes
       that are known to take place in the nuclei of
       apparently normal cells found near cancer tissue. In
       addition, MACs have been detected in tissue found near
       pre-cancerous lesions. Because the cells exhibiting
       MACs are more numerous than the malignant cells, MACs
       offer an additional way of diagnosing the presence of

cancer, especially in cases where no cancerous cells can be located" (paragraph bridging pages 1 and 2).

2.   The prior art

2.1   D1
       The appellant accepts that D1 discloses the features
       contained in the preamble of claim 1. Multivariate
       analysis is referred to at column 5, line 16 onwards,
       and is said to comprise "cluster analysis leading to a
       decision tree made up of thresholds and discriminant
       functions". There is no mention of classifiers.

2.2   D2

       D2 is concerned with the detection of nuclei of
       abnormal cells, in particular cancerous and
       precancerous cells (cf. claim 9). It does not
       explicitly concern MACs. The detection of normal and
       abnormal cells is performed automatically by means of a
       classifier (cf. page 8, line 20 to page 10, line 10).

The main request

3.   Claim 1

3.1   The invention being a method of detecting malignancy-
       associated changes in cells, the question whether or
       not it constitutes a diagnostic method in the sense of
       Article 52(4) EPC would normally have to be
       investigated. However, in the present circumstances no
       answer to this question is required since, as set forth
       below, the invention does in any case not involve an
       inventive step.

3.2   The examining division held that D1 anticipated the
        invention because it suggested using *a posteriori*
        clinical knowledge of the patients' medical history
        (decision, point 3). This could be concluded from the
        definition of MACs in D1 as "changed nuclear features
        of ostensibly normal cells growing in the vicinity of
        the cancerous or precancerous lesion compared to those
        of normal cells from the same type of tissue of a
        normal, healthy individual" (column 2, lines 19 to 25).
        The examining division thus considered that knowledge
        of cells exhibiting MAC as well as cells not exhibiting
        MAC was necessary in order to identify discriminant
        features.

3.3   The appellant has argued that since D1 does not mention
        a classifier constructed from two databases comprising
        features from healthy and abnormal patients,
        respectively, the cluster analysis mentioned in D1
        would not involve using cells from a healthy patient.
        If it did it would lead to a diagnosis of "not-normal"
        rather than "exhibits MAC", which would seem
        nonsensical (cf. letter dated 25 August 2006).

3.4   The Board finds the argumentation of the examining
        division convincing. It would indeed appear strange if
        abnormal changes could be identified without knowledge
        of the normal state, and the Board cannot see how D1
        could possibly be interpreted along the lines suggested
        by the appellant. A classifier constructed from
        "normal" and "abnormal" cell databases in accordance
        with claim 1 is therefore to be regarded as implicitly
        disclosed in D1. On the basis of this understanding all
        features of claim 1 are known from this document.

3.5   Moreover, as pointed out in the decision under appeal
        (point 3), a classifier constructed from a training
        database containing normal and abnormal cells is known
        from D2 (page 9, line 32 to page 10, line 4).

        The appellant has observed that D2 is concerned with
        the detection of cancer cells rather than MACs, but
        this is in the Board's view no reason for ignoring the
        document. Cytologists working with MACs must be assumed
        to take an interest in any method used for
        categorization of cells or cell nuclei, and
        particularly methods for diagnosing cancer.

        The appellant has further argued that in D2 there is no
        consideration of a population of (apparently) normal
        cells in both healthy and cancerous patients. But this
        difference merely reflects the fact that D2 is
        concerned with malignant cells, not with cells
        exhibiting MACs. It goes without saying that the
        training databases must be chosen in accordance with
        the purpose of the detection.

        The Board thus concludes, as did the examining division,
        that if the skilled person found the indications in D1
        insufficient he would consult D2. This document would
        lead him to apply a classifier constructed from a first
        database comprising feature values of normal cells
        (obtained from apparently normal cells of a healthy
        patient) and a second database comprising feature
        values of abnormal cells (such obtained from apparently
        normal cells of a cancer patient) to the method of
        detecting MACs described in D1.

3.6   It follows that the subject-matter of claim 1 in any
        case does not involve an inventive step having regard
        to the teachings of D1 and D2 (Article 56 EPC), even if
        novelty were accepted by ignoring the fact that
        features of the claim appear to be implicitly disclosed
        in D1.

4.   Claim B

4.1   Claim B is directed to a classifier. With reference to
        figure 8 of the application, the description explains
        that "a classifier 290 is a computer program that
        analyzes an object based on its feature values"
        (page 11, lines 21,22). Decision T 1173/97 (OJ EPO
        1999,609) states that a computer program is not
        excluded from patentability under Article 52(2) and (3)
        EPC if it is capable of producing a "further technical
        effect" which goes beyond the normal physical
        interactions between program and computer (see the
        headnote). The Board needs however not to investigate
        whether the classifier of claim B produces such a
        further technical effect since, for the reasons
        indicated below, its subject-matter is in any case
        obvious.

4.2   Claim B recites the classifier features contained in
        claim 1 with the addition that data from the databases
        is used to develop a discriminant function that can
        discriminate between MAC-positive nuclei and MAC-
        negative nuclei. The feature "discriminant function" is
        not regarded as a further limitation since it is merely
        the name given for the set of rules used for detecting
        MACs. This interpretation is in line with the
        appellant's statement that claim B "claims the same

invention /as claim 1/" (letter dated 25 August 2006).
Thus this claim must share the fate of claim 1. It may
also be noted that D1 employs the expression
"discriminant function" as well (column 5, lines 16
to 21).

5.   It follows that the main request is refused.

Auxiliary requests 1-4, 8 and 10

6.   Claim 1 of auxiliary request 1 is identical with
        claim 1 of the main request. Auxiliary requests 2 to 4,
        8 and 10 contain claim B. These requests are therefore
        also not allowable.

Auxiliary requests 5-7

7.   Claim 1 according to auxiliary requests 5 to 7 all
        contain the feature "determining the need for further
        investigation if the ratio exceeds the predetermined
        threshold". This feature has no basis in the
        application as originally filed. The description
        mentions that "/i/f the frequency of cells exhibiting
        MACs exceeds the threshold, the computer system can
        indicate that the patient is healthy at step 342 or
        likely has or will develop cancer" (page 13,lines 6
        to 9). Probable as it may be that a physician will
        determine the need for further investigation if a
        patient has been found likely to develop cancer, this
        is in fact not stated. Therefore this feature has been
        added in contravention of Article 123(2) EPC and the
        requests must be refused.

8.   It might be added that since the subject-matters
        claimed do not differ significantly from the invention
        of the main request, they are in the Board's view in
        any case unlikely to involve an inventive step.

Auxiliary request 9

9.   Claim A according to auxiliary request 9 differs from
        claim 1 of the main request in that values in the
        second database are obtained from a "cancer patient"
        (rather than an "abnormal patient"). This amendment
        cannot overcome the objections against the main request
        since both D1 and D2 are concerned with the diagnosis
        of cancer. Thus this request must also be refused.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

P. Cremona   S. Steinbrener

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