

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 18

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte PRESCOTT DEININGER and DAVID KASS

Appeal No. 2001-1949
Application No. 08/958,009

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and GRIMES, Administrative Patent Judges.

GRIMES, 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 3-12, all of the claims remaining. Claim 9 is representative and reads as follows:

9. A process of estimating ethnic affiliation, the process comprising:
 - A. providing a DNA sample from a human, the sample containing DNA having Alu U and Alu D regions; and
 - B. determining haplotypes within the Alu U and Alu D regions; and
 - C. estimating the ethnic affiliation of the human from the discrimination coefficient for each ethnic group.

The examiner relies on the following references:

Shriver et al. (Shriver), "Ethnic-affiliation estimation by use of population-specific DNA markers," American Journal of Human Genetics, Vol. 60, pp. 957-964 (1997)

Batzer et al. (Batzer), "Genetic variation of Recent Alu Insertions in Human Populations," Journal of Molecular Evolution, Vol. 42, No. 1, pp. 22-29 (1996)

Yamamoto et al. (Yamamoto), "The Human LDL Receptor: A Cysteine-Rich Protein with Multiple Alu Sequences in its mRNA," Cell, Vol. 39, pp. 27-38 (1984)

Cotton, "Detection of Mutations in DNA," Current Opinion in Biotechnology, Vol. 3, pp. 24-30 (1992)

Claims 3-6 and 8-12 stand rejected under 35 U.S.C. § 103 as obvious over the combined teachings of Shriver, Batzer, and Yamamoto.

Claims 3-12 stand rejected under 35 U.S.C. § 103 as obvious over the combined teachings of Shriver, Batzer, Yamamoto, and Cotton.

We reverse.

Background

According to Appellants' specification,

[a] need exists for characterized human nuclear loci that could be analyzed for diversity in a reasonably rapid way. Such diversity, or polymorphism, is useful for establishing human identity, often for forensic purposes. In addition, diversity is useful for establishing parentage.

Page 1. The specification also discloses that most regions of the human genome

show so little diversity that analysis requires sequencing of very long genomic regions to be informative. Regions of the genome that are hypervariable overcome this difficulty by allowing a significant amount of sequence variation in a shorter DNA sequence, providing a tremendous benefit for studies of human diversity.

Id., pages 1-2.

The specification discloses that a region of the low density lipoprotein receptor (LDLR) gene shows a high degree of sequence diversity. In particular, the 3' untranslated region of the LDLR gene contains two Alu sequences,¹ known as Alu U and Alu D, which are disclosed to show a high level of diversity. See id., pages 15-16. When Appellants sequenced the Alu U element in people from different ethnic groups, they found that

out of the 14 individuals . . . sequenced across this one Alu region, there are 12 different alleles. . . They diverge from the consensus at about 1% of the bases within the body of the Alu (excluding the normally variable A tail also). This represents about 50 times the diversity of other typical neutral human DNA sites.

Id., page 15. Alu D showed a lower, but still considerable, level of diversity. See id., page 16. According to the specification, the degree of variability in the Alu U and Alu D elements

indicates a rate of evolution of approximately 100 times that of other human nuclear loci. For the entire region, no two human sequences were identical, in contrast to the virtual monomorphism at other nuclear loci. This level of diversity and rate of evolution make this highly polymorphic region useful for forensic analysis. The rapid evolution of this locus means that the allelic SNPs [single nucleotide polymorphisms] have not had time to approach equilibrium. Thus, haplotypes are associated with ethnic origins.

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Discussion

Claim 9 is directed to a method of estimating ethnic affiliation by comparing the sequence of an individual's Alu U and Alu D regions with the

¹ "Alu sequences comprise a family of generally nonfunctional processed pseudogenes. Alu elements are DNA sequences that are approximately 300 bp long that belong to a family of repeated sequences. Alu family members appear more than 500,000 times in the human genome, comprising 5-6% of the genome." Specification, pages 3-4.

sequences commonly found in different ethnic groups. The examiner rejected claim 9, together with claims 3-6, 8, and 10-12, as obvious in view of Shriver, Batzer, and Yamamoto.

The examiner characterized Shriver as teaching a method of estimating ethnic affiliation based on DNA variations, using “allelic sequences present in microsatellite repeat sequences or RFLP sequences.” Examiner’s Answer, page 4. He cited Batzer as teaching a similar process for estimating ethnic affiliation based on DNA sequences, using “allelic sequences present in an Alu repeat sequence.” Id.

The examiner acknowledged that the methods disclosed by Shriver and Batzer did not use the Alu U or Alu D sequences, but he noted Yamamoto “teaches the Alu U and Alu D sequences.” He concluded that

[i]t would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the ethnic affiliation methods of Shriver et al[.] in view of Batzer et al [.] with the use of the Alu sequence as taught by Yamamoto.

Id., page 6. The examiner found that a skilled artisan would have been motivated to combine the cited references because Yamamoto’s Alu sequences are “structurally and functionally alternative” to both the other Alu sequences used by Batzer and the microsatellite repeats used by Shriver. See id.

Appellants argue that the examiner’s rejection is based on impermissible hindsight. See the Appeal Brief, page 14:

Shriver [and] Batzer could not have used the present invention without knowledge of the polymorphisms of the 950 bp LDL[R] sequence that contains Alu U and Alu D. For Shriver to combine his method with the observation of Yamamoto would require that he

blindly choose the Yamamoto sequence from among the 4 billion alternative bases within the human genome. Likewise, Batzer would have had to choose the Yamamoto sequence from among the 500,000 Alu sequences found within the human genome. The Yamamoto sequence was the first example of the sequence utilized in the present invention; it is limited to the sequence from a single individual, and thus without significance for any polymorphism at the locus in question.

Appellants also argue that they have shown unexpectedly superior results compared to the prior art. See the Appeal Brief, pages 12-13.

“In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness.” In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). “[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.” In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992).

We agree with Appellants that the examiner has not made out a prima facie case of obviousness. The claims are directed to a method of estimating or determining ethnic affiliation by measuring variability at two specific, discrete genetic loci—Alu U and Alu D. The references cited by the examiner show that methods were known in the art for estimating or determining ethnic affiliation by analyzing genetic variability (Shriver and Batzer), and that the existence of the Alu U and Alu D sequences was known (Yamamoto). However, there is nothing disclosed in any of the relied-on references that would have suggested to those of skill in the art that the Alu U and Alu D sequences, as opposed to any of the

other 500,000 Alu sequences in the human genome, would have been useful in a method for determining or estimating ethnic affiliation.

“[I]dentification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant.” In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000). That is, the record must show evidence that “a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.” In re Rouffet, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1458 (Fed. Cir. 1998).

Such evidence is lacking here. The examiner’s stated basis for combining Yamamoto’s Alu U and Alu D elements with the methods of Shriver and Batzer is that Alu U and Alu D are “structurally and functionally alternative” to the loci analyzed by Shriver and Batzer. We take this to mean that those of skill in the art would have recognized the equivalence of all Alu elements for use in a method based on DNA variability. The examiner cites no evidence to support this position, and in fact the evidence of record is to the contrary.

The specification states that some Alu repeats show no or only minor variation among humans. See page 14:

Three different neutral nuclear loci, comprising 55 kb total, that encompass Alu repeats have been sequenced for multiple representatives of diverse human population groups. Most individuals and populations showed absolutely no variation in these three loci.

By contrast, the Alu U and Alu D elements recited in the claims showed a high degree of heterogeneity. See the specification, page 15 (Alu U shows “about 50 times the diversity of other typical neutral human DNA sites.”); page 16 (The region of the LDLR gene comprising Alu U and Alu D “has maintained a higher level of variation than other known nuclear regions. . . . [D]ifferences within the region among human populations . . . show a high level of diversity.”); page 25 (“For the entire region, no two human sequences were identical, in contrast to virtual monomorphism at other nuclear loci.”); and page 26 (“Thus, there is a hot-spot for diversity, with the flanking sequences showing relatively low allelic diversity much like most other neutral nuclear loci, such as introns or pseudogenes.”).

In addition, we note that the claims are directed to a method requiring analysis of only two genetic loci, Alu U and Alu D. The methods disclosed by Shriver and Batzer, by contrast, involved analysis of different types and/or larger numbers of genetic loci. Batzer based his conclusions on an analysis of the presence or absence of six different Alu sequences among members of different ethnic groups. See page 24 (“The distribution of six individual polymorphic Alu insertions was determined in a total of 563 unrelated individuals that comprised

14 population groups.”).² Shriver presents a set of twenty genetic loci that can serve as “population-specific alleles” for ethnic-affiliation estimation of African-Americans and a different set of twenty genetic loci for ethnic-affiliation estimation of Hispanic-Americans. See Tables 1 and 2.

None of the references relied on by the examiner teaches or suggests that the Alu U and Alu D elements differ in sequence between different ethnic groups. The examiner has pointed to no evidence that those skilled in the art would have been led to practice a method of predicting or determining ethnic affiliation by analyzing differences in the sequences of the two specific genetic loci recited in the claims, with a reasonable expectation of success.

We conclude that, while methods for genetically determining or predicting ethnicity were known, and the existence of the Alu U and Alu D elements was known, the prior art provides no suggestion or motivation to combine the method with the Alu elements. “Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor’s disclosure as a blueprint for piecing together the prior art to defeat patentability—the essence of hindsight.” In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). Since we conclude that the examiner has not made out a prima facie case, we need not address Appellants’ rebuttal evidence.

² Batzer refers to the Alu elements as “polymorphic,” but appears to use this phrase to refer to variability in the presence/absence of a particular element within a population, rather than using it to refer to differences in the sequence of the particular Alu element. See, e.g., page 24, right-hand column (“Each Alu insertion was polymorphic in all of the populations except for the D1 repeat, which was not found within a small sample of Nigerians.”).

The examiner also rejected all of the claims as obvious over the combination of Shriver, Batzer, Yamamoto, and Cotton. Shriver, Batzer, and Yamamoto were relied on for the same teachings discussed above. We have concluded, above, that these references do not support a prima facie case of obviousness with respect to claims 3-6 and 8-12. The examiner cited Cotton only with regard to a specific limitation of claim 7. Since the cited references do not render obvious independent claim 3, then a fortiori, they do not render obvious the claims that depend on claim 3, including claim 7. The rejection over Shriver, Batzer, Yamamoto, and Cotton is reversed for the reasons discussed above.

Summary

The examiner has not adequately shown that the prior art would have suggested the claimed method to those of ordinary skill in the art. The rejections under 35 U.S.C. § 103 are reversed.

REVERSED

Sherman D. Winters)	
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