Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.
DECISION ON APPEAL

This is an appeal\(^1\) under 35 U.S.C. § 134 involving claims to an antiviral pharmaceutical composition. The Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

\(^1\) Appellants identify the Real Party in Interest as the Board of Trustees of the University of Arkansas (see Br. 3).
Statement of the Case

Background

“[C]ompounds and methods for inhibiting HCV replication are needed. Methods of identifying compounds that inhibit HCV replication are also needed” (Spec. 2, l. 31–3, l. 2).

The Claims

Claims 10, 15, 32, and 35–38 are on appeal. Independent claim 10 is representative and reads as follows:

10. A pharmaceutical composition comprising:
    a compound of molecular weight 10,000 or less,
    wherein the compound interacts with NS3 to inhibit NS3 oligomerization and wherein the compound inhibits hepatitis C virus (HCV) replication;
    wherein the compound consists of SEQ ID NO:1; and
    a pharmaceutically acceptable diluent.

The Issues

A. The Examiner rejected claims 10 and 36–38 under 35 U.S.C. § 103(a) over Sette3 (Ans. 5–10).
B. The Examiner rejected claims 15 and 35 under 35 U.S.C. § 103(a) over Sette, Kim4, Beerens5, Bishop6, and Arai7 (Ans. 11–14).

2 Claims 1–9, 11–14, 16–31, 33, and 34 were cancelled (Br. 3).
4 Kim et al., Introduction of Soluble Proteins into the MHC Class I Pathway by Conjugation to an HIV tat Peptide, 159 J. IMMUN. 1666–1668 (1997).
5 Beerens et al., Protein Transduction Domains and their Utility in Gene Therapy, 3 CURRENT GENE THER. 486–494 (2003).

A. 35 U.S.C. § 103(a) over Sette

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that Sette renders claims 10 and 37 obvious?

Findings of fact

1. The Specification teaches “a peptide having the sequence HIDAHFLSQTK [as] (SEQ ID NO:1)” (Spec. 14, l. 2).

2. The Specification teaches “a peptide comprising the reverse D analog of SEQ ID NO:1 . . . (or a portion thereof, e.g., at least 4 contiguous residues), where the amino acids are D isomers instead of L isomers” (Spec. 14, ll. 5–9).

3. Sette teaches that “[t]his invention uses our knowledge of the mechanisms by which antigen is recognized by T cells to identify and prepare HCV epitopes, and to develop epitope-based vaccines directed towards HCV” (Sette, Abstract).

4. Sette teaches that:

   there has existed a need for peptide epitopes that are bound by multiple HLA antigen molecules for use in epitope-based vaccines. The greater the number of HLA antigen molecules bound, the greater the breadth of population

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7 Arai et al., Design of the linkers which effectively separate domains of a bifunctional fusion protein, 14(8) PROTEIN ENGINEERING 529-532 (2001).
8 Regenmortel et al., D-peptides as immunogens and diagnostic reagents, 9 CURRENT OPINIONS IN BIOTECH. 377–382 (1998).
coverage by the vaccine . . . Furthermore, as described herein in greater detail, a need has existed to modulate peptide binding properties, for example, so that peptides that are able to bind to multiple HLA antigens do so with an affinity that will stimulate an immune response . . . [E]pitopes for inclusion in vaccine compositions of the invention are selected by a process whereby protein sequences of known antigens are evaluated for the presence of motif or supermotif-bearing epitopes . . . Supermotif-bearing peptides may additionally be tested for the ability to bind to multiple alleles within the HLA supertype family. The invention also includes an embodiment comprising a method for monitoring or evaluating an immune response to HCV in a patient having a known HLA-type, the method comprising incubating a T lymphocyte sample from the patient with a peptide composition comprising an HCV epitope consisting essentially of an amino acid sequence described in Tables VII to Table XX or Table XXII which binds the product of at least one HLA allele present in said patient, and detecting for the presence of a T lymphocyte that binds to the peptide.

(Sette, 6, l. 3 to 7, l. 1).

5. Sette teaches that the “identification of motifs and/or supermotifs that correlate with high and intermediate affinity binding is an important issue with respect to the identification of immunogenic peptide epitopes for the inclusion in a vaccine” (Sette 20, ll. 11–14).

6. Sette teaches that the Kast study “demonstrates the value of motifs for the identification of peptide epitopes for inclusion in a vaccine: application of motif-based identification techniques eliminates screening of 90% of the potential epitopes in a target antigen protein sequence. Such peptide epitopes are identified in the Tables” (Sette 20, ll. 23–27).
7. Sette teaches that:

To obtain the peptide epitope sequences listed in each Table, protein sequence data from fourteen HCV isolates were evaluated for presence of the designated supermotif. . . . Peptide epitopes were additionally evaluated on the basis of their conservancy among these fourteen strains. . . . A criterion for conservancy requires that the entire 9-mer region of an HLA class II binding peptide be totally conserved in 79% of the sequences available for a specific protein. The percent conservancy of the selected peptide epitopes is indicated on the Tables. The frequency, i.e. the number of strains of the fourteen strains in which the totally conserved peptide sequence was identified, is also shown.

(Sette 21, l. 26 to 22, l. 4).

8. Sette teaches that “[t]he HLA-A3 supermotif is characterized by the presence in peptide ligands of A, L, I, V, M, S, or, T as a primary anchor at position 2, and a positively-charged residue, R or K, at the C-terminal position of the epitope” (Sette 23, ll. 21–31).

9. Sette teaches that “[t]he HLA-A3 motif is characterized by the presence in peptide ligands of L, M, V, I, S, A, T, F, C, G, or D as a primary anchor residue at position 2, and the presence of K, Y, R, H, F, or A as a primary anchor residue at the C-terminal position of the epitope. . . . Peptide epitopes that comprise the A3 motif are set forth in Table XVI. Peptide epitopes that also comprise the A3 supermotif are also listed in Table IX” (Sette 27, ll. 25–34).
10. Table XVI of Sette is reproduced in relevant part below:

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Position</th>
<th>No. of Amino Acids</th>
<th>Sequence Frequency</th>
<th>Conservancy (%)</th>
<th>A*0301</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDH/FL502K</td>
<td>1572</td>
<td>11</td>
<td>14</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>14H/PTGSKK</td>
<td>1233</td>
<td>10</td>
<td>12</td>
<td>80</td>
<td>0.5900</td>
</tr>
</tbody>
</table>

(Sette 156).

11. Table IX of Sette is reproduced in relevant part below:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>14</td>
<td>1572</td>
<td>HDH/FL502K</td>
<td>0.5900</td>
<td>0.0024</td>
<td>0.0005</td>
<td>0.0008</td>
<td>0.0028</td>
</tr>
<tr>
<td>86</td>
<td>12</td>
<td>1233</td>
<td>14H/PTGSKK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Sette 119).

12. Sette teaches that "[t]he HLA–A11 motif is characterized by the presence in peptide ligands of V, T, M, L, I, S, A, G, N, C, D, or F as a primary anchor residue in position 2, and K, R, Y, or H as a primary anchor residue at the C-terminal position of the epitope . . . . Representative peptide epitopes that comprise the A11 motif are set forth on the attached Table XVII; peptide epitopes comprising the A3 allele-specific motif are also present in this Table because of the extensive overlap between the A3 and A11 motif primary anchor specificities" (Sette 28, ll. 3–10).

13. Table XVII of Sette is reproduced in relevant part below:

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Position</th>
<th>No. of Amino Acids</th>
<th>Sequence Frequency</th>
<th>Conservancy (%)</th>
<th>A*1101</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDH/FL502K</td>
<td>1572</td>
<td>11</td>
<td>14</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>14H/PTGSKK</td>
<td>1233</td>
<td>10</td>
<td>12</td>
<td>80</td>
<td>0.0024</td>
</tr>
</tbody>
</table>

(Sette 167).
Principles of Law

“The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.”


Analysis

We adopt the Examiner’s findings of fact and reasoning regarding the scope and content of the prior art (Ans. 5–10; FF 1–13) and agree that the claims are rendered obvious by Sette. We address Appellants’ arguments below.

Appellants contend with respect to claim 10 that

Sette does not disclose any pharmaceutical utility for SEQ ID NO:1, not even utility as a vaccine (which is disclosed for other HCV peptides but not HIDAHFLSQTK), and thus does not disclose or suggest a pharmaceutical composition comprising HIDAHFSQTK (SEQ ID NO:1) and a pharmaceutically acceptable diluent, as is recited in claim 10.

The Examiner’s position is that because SEQ ID NO:1 is disclosed in Sette, even though no pharmaceutical utility, including any utility as a vaccine, is disclosed for it, that constitutes an anticipation of a claim to a pharmaceutical composition comprising the peptide and a pharmaceutically acceptable diluent . . . . The Examiner concedes that “Sette et al. is interested in these peptide motifs for the identification of peptide epitopes (e.g., CTL inducing peptide epitopes) for inclusion in vaccines (e.g., a pharmaceutical use).” (Page 5 of Office Action mailed January 17, 2012.) But then she ignores the fact that Sette rules out this particular peptide for inclusion in vaccines, because Sette et al. did not include it in Tables XXVI-XXIX and XXXII, which are the only ones it says are suitable as vaccines. (Page 45, lines 15–16.) The Examiner further concedes “Sette et al. . . . does not suggest using this sequence [SEQ ID NO:1] for immunization or in pharmaceutical compositions.” (Page 6, of the Office Action
mailed January 17, 2012). That should be the end of the analysis. That statement proves that claim 10 is not obvious over by Sette.

(Br. 7).

We are not persuaded. First, Appellants’ reference to an anticipation rejection, and to the Examiner’s position in the office action mailed January 17, 2012, are moot as they are not germane to the instant obviousness rejection and/or the current position taken by the Examiner.9

We find that the evidence supports the Examiner’s position regarding pharmaceutical utility for SEQ ID NO:1. Sette teaches selecting epitopes for inclusion in a vaccine by identifying HCV epitopes motifs or supermotifs (FF 4–6). Sette teaches that “application of motif-based identification techniques eliminates screening of 90% of the potential epitopes in a target antigen protein sequence”, and that such desirable “peptides epitopes are identified in the Tables described below” (FF 6), including Tables IX, XVI and XVII, which each disclose SEQ ID NO:1 (FF 1, 10, 11, 13).

Sette teaches a “method for monitoring or evaluating an immune response to HCV in a patient having a known HLA-type . . . with a peptide composition comprising an HCV epitope consisting essentially of an amino acid sequence described in Tables VII to Table XX”, wherein, again, Table

9 “There is nothing unusual, certainly, about an examiner changing his viewpoint as to the patentability of claims as the prosecution of a case progresses, and, so long as the rules of Patent Office practice are duly complied with, an applicant has no legal ground for complaint because of such change in view. The life of a patent solicitor has always been a hard one.” In re Ruschig, 379 F.2d 990, 993 (CCPA 1967).
IX discloses SEQ ID NO:1 (FF 11). Sette further teaches that “protein sequence data from fourteen HCV isolates were evaluated for presence of the designated supermotif”, and “were additionally evaluated on the basis of their conservancy among these fourteen strains”, and reports in Table XVI 100% conservancy for SEQ ID NO:1 among all fourteen strains (FF 7, 10). Sette further identifies SEQ ID NO:1 as having both the HLA-A3 motif (in Table XVI), the HLA-A3 supermotif (in Table IX), and HLA-A 11 motif (in Tables XVII) (FF 8–13).

We recognize, but do not find persuasive, Appellants’ contention that “Sette concerns vaccines against HCV, and discloses that epitopes listed in Tables XXVI-XXIX and XXXII may be utilized in a vaccine, but the cited sequence is not in these tables” (Br. 6; emphasis in the original).

While Appellants are correct that Sette did not choose the peptide of SEQ ID NO:1 for further testing, Sette did specifically identify SEQ ID NO:1 by computer screening as containing an epitope with the HCV motifs necessary for inclusion in vaccine compositions (FF 7–13). Each the listed peptides identified by Sette’s screening would have been expected by Sette to function as an antigen in a vaccine (FF 4–13). “If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.” KSR at 417.

Conclusion of Law

The evidence of record supports the Examiner’s conclusion that Sette renders claims 10 and 37 obvious.
B. 35 U.S.C. § 103(a) over Sette, Kim, Beerens, Bishop, and Arai

The issue with respect to this rejection is:

(i) Does the evidence of record support the Examiner’s conclusion that Sette, Kim, Beerens, Bishop, and Arai render claims 15 and 35 obvious?

(ii) Have Appellants presented evidence of secondary considerations, that when weighed with the evidence of obviousness, is sufficient to support a conclusion of non-obviousness?

Findings of Fact

14. Kim teaches that

Protection against most intracellular pathogens requires T cells that recognize pathogen-derived peptides in association with MHC class I molecules on the surface of infected cells. However, because exogenous proteins do not ordinarily enter the cytosol and access the MHC class I-processing pathway, protein-based vaccines that induce class I-restricted CTL responses have proved difficult to design. We have addressed this problem by conjugating proteins, such as OVA, to a short cationic peptide derived from HIV-1 tat (residues 49-57). When APC were exposed in vitro to such protein conjugates, they processed and presented the peptides in association with MHC class I molecules and stimulated CD8+ Ag-specific T cells. Moreover, Ag-specific CTLs were generated in vivo by immunizing mice with histocompatible dendritic cells that had been exposed to protein-tat conjugates.

(Kim, Abstract).

15. Beerens teaches that “[t]he minimal PTD [protein transduction domain] of TAT has been identified as a 9 amino acid (aa) sequence . . . (TAT₄⁹-₅₇)” (Beerens 487, col. 1).
16. Beerens teaches that “[s]everal peptides have been synthesized in attempt to create more potent PTDs . . . . Many of these synthetic PTDs are based on existing and well documented peptides . . . . A few of these synthetic PTDs showed better translocation properties then the existing ones. Some interesting synthetic PTDs are mentioned in Table 2” (Beerens, 488, col. 2; emphasis in the original).

17. Table 2 of Beerens is reproduced in relevant part below:

<table>
<thead>
<tr>
<th>Name</th>
<th>Origin</th>
<th>Efficiency</th>
<th>Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTD-4</td>
<td>TetPTD [He et al., 2001]</td>
<td>33% TetPTD</td>
<td>Y A R A R A A R Q A R R E</td>
</tr>
<tr>
<td>PTD-4</td>
<td>Y G R K R Q R R E</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Beerens 488).

18. Bishop teaches “the peptide Rad51C”, wherein in Figure 2B “[a] three-residue glycine linker connects the RAD51C-derived and peptide transduction segments” as follows:

Rad51C(D1425)-PTD4: LVMPFLEAVLVR - GGG - YARAAARQARA
Rad51C(serm)-PTD4: SVAFLLESeVP - GGG - YARAAARQARA

(Bishop 6).

19. Dowdy teaches “an anti-pathogen system that kills or injures pathogen-infected cells by introducing into the cells a fusion protein comprising a protein transduction domain and a cytotoxic domain” (Dowdy, col. 1, ll. 16–19).

20. Dowdy teaches a “protein transduction domain . . . wherein the transduction domain consists of . . . YARAAARQARA (SEQ ID NO. 4)” (Dowdy, claims 18).
21. Arai teaches that “linkers can effectively separate the domains of fusion proteins and the distance between the domains can be controlled by changing the repetitions” (Arai 531, col. 2).

Analysis

We adopt the Examiner’s findings of fact and reasoning regarding the scope and content of the prior art (Ans. 11–14; FF 14–21) and agree that the claims are rendered obvious by Sette, Kim, Beerens, Bishop, and Arai. We address Appellants’ arguments below.

Appellants contend that Dowdy provides no motivation to modify Sette by attaching a protein transduction domain to the present SEQ ID NO:1 . . . . Dowdy teaches fusing a protein transduction domain to a cytotoxic domain, not to a peptide for use as a vaccine, much less to a peptide that has no pharmaceutical utility. Accordingly, Dowdy provides no suggestion or motivation to modify Sette to attach Dowdy’s SEQ ID NO:4 to the present SEQ ID NO:1 to arrive at the present SEQ ID NO:2 . . . . Kim only suggests adding a tat translocation peptide to proteins, not to short peptides. It states that exogenous proteins do not ordinarily enter the cytosol . . . . [T]he Examiner has made no comments about Arai and Applicants cannot see any relevance to it (Br. 10; emphasis in the original).

We are not persuaded. Appellants provide no reason, based on evidence, as to why amino acid chain length matters here. While a peptide is a short amino acid chain (HIDAHFSQTK is 10 amino acids in length), and a protein is usually a longer amino acid chain, Kim expressly teaches that TAT assists in translocation of amino acid chains for inducing immune
response as required by vaccines (FF 14). Bishop evidences that such transduction segments may be linked to 12 amino acid peptide sequences (FF 18). Thus, the Examiner relies upon the combination of Kim and Bishop to demonstrate the desirability of transduction domains for immunogens such as Sette’s peptide as well as the ability to link transduction domains to peptides as well as proteins (FF 14, 18). See In re Merck & Co., Inc., 800 F.2d 1091, 1097 (Fed. Cir. 1986) (“Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. . . . [The reference] must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole.”).

Appellants further provide no support, by way of evidence or argument, for the statement that “[h]ad a prima facie case of obviousness been established, it would be rebutted by the unexpected result that the recited peptide interacts with NS3 to inhibit NS3 oligomerization and inhibits hepatitis C virus replication” (Br. 11). Appellants have merely discovered a previously unappreciated property of a prior art composition, and this does not render the old composition patentably new to the discoverers. See Atlas Powder Co. v. Ireco, Inc., 190 F.3d 1342, 1347 (Fed. Cir. 1999). The claiming of an unknown property that is inherently present in the prior art does not make the present claims patentable. See In re Best, 562 F.2d 1252, 1254 (CCPA 1977).

Conclusion of Law

(i) The evidence of record support the Examiner’s conclusion that Sette, Kim, Beerens, Bishop, and Arai render claims 15 and 35 obvious.
(ii) Appellants have not presented evidence of secondary considerations, that when weighed with the evidence of obviousness, is sufficient to support a conclusion of non-obviousness.

C. 35 U.S.C. § 103(a) over Sette and Regenmortel

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that Sette and Regenmortel render claim 32 obvious?

Findings of Fact

22. Regenmortel teaches that “[t]here has been a regain of interest in the immunological applications of peptides assembled partly or totally from D-amino acids. Such peptides are much more stable to proteolysis than natural L-peptides and they have considerable potential as synthetic vaccines and as immunomodulators in T-cell responses” (Regenmortel, Abstract).

23. Regenmortel teaches that retro-all-D RI peptide analogues of the immunodominant epitope located in residues 141–159 of the VP1 protein . . . of foot-and-mouth disease were synthesized and used to raise antibodies in rabbits . . . The R1 peptides led to higher serum antibody titers that appeared earlier after the start of immunization and lasted longer than those obtained with the correspondig L-peptides. . . . Antibodies to the R1 peptides cross-reacted strongly with L-peptides and virus particles.

(Regenmortel 380, col. 2).

Analysis

We adopt the Examiner’s findings of fact and reasoning regarding the scope and content of the prior art (Ans. 14–15; FF 22–23) and agree that the
claims are rendered obvious by Sette and Regenmortel. We address Appellants’ arguments below.

Appellants contend that “[e]ven if Sette had disclosed that SEQ ID NO:1 is useful as a vaccine, which it does not, the results of using it or a reverse D analogue of SEQ ID NO:1 are unexpected: it is shown to inhibit HCV replication and to do so by inhibiting NS3 oligomerization. Both of those results are unexpected and entirely unpredictable based on Sette and Regenmortel” (Br. 12).

We are not persuaded because Regenmortel teaches that “[a]ntibodies to the R1 peptides cross-reacted strongly with L-peptides and virus particles” (FF 23). Thus, the result inherently obtained with SEQ ID NO:1 of Sette would have been expected to remain present when modified as suggested by Regenmortel, because Regenmortel evidences that modification with the retro-all-D peptides retains immunogenicity for vaccine compositions (FF 23).

Conclusion of Law

The evidence of record support the Examiner’s conclusion that Sette and Regenmortel render claim 32 obvious.

SUMMARY

We affirm the rejection of claims 10 and 37 under 35 U.S.C. § 103(a) as obvious over Sette. Claims 36 and 38 fall with claims 10 and 37. 37 C.F.R. § 41.37(c)(1)(iv).

We affirm the rejection of claims 15 and 35 under 35 U.S.C. § 103(a) as obvious over Sette, Kim, Beerens, Bishop, and Arai.
We affirm the rejection of claim 32 under 35 U.S.C. § 103(a) as obvious over Sette and Regenmortel.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED