

# CRISPR HAS ALREADY REVOLUTIONIZED GENETICS, WHY NOT THE OBVIOUSNESS STANDARD TOO?

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## I. INTRODUCTION

Throughout history humanity has transformed and adapted to the world's various climates.<sup>1</sup> One of the methods humanity has employed to adapt to the world is known as artificial selection.<sup>2</sup> The first farmers would choose the seeds of plants that produced the most favorable traits, such as the plant with the most fruit, to plant in the following season.<sup>3</sup> Over many years, this selection process produced domesticated plants that bore little resemblance to wild plants.<sup>4</sup> As human industry developed and science advanced concurrently, favorable and unfavorable traits were found to be controlled by genes.<sup>5</sup> The biotechnology industry emerged as methods to artificially select genes controlling these traits were discovered.<sup>6</sup> The methods, however, were tedious and expensive. In the last decade, a new technology has emerged known as CRISPR-Cas9 (“CRISPR”).<sup>7</sup> This new technology allows humanity to accelerate the artificial selection process by editing the genome of organisms in a quicker and less expensive way than previous technologies.<sup>8</sup> The economic benefit of this technology is enormous.<sup>9</sup> In fact, market forecasts estimate that by 2020, the Genome Editing market will be worth

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1. Nathanael Massey, *Humans May Be the Most Adaptive Species*, SCIENTIFIC AMERICAN (Sept. 25, 2013), <https://www.scientificamerican.com/article/humans-may-be-most-adaptive-species/> [<https://perma.cc/R9LH-TSXQ>].

2. Andrea Becker, *Describe the Process of Artificial Selection*, SCIENCING (Apr. 25, 2017), <https://sciencing.com/describe-process-artificial-selection-16957.html> [<https://perma.cc/NB2Z-3YNX>].

3. Gabriel Rangel, *From Corgis to Corn: A Brief Look at the Long History of GMO Technology*, HARVARD SCIENCE IN THE NEWS BLOG (Aug. 9, 2015), <http://sitn.hms.harvard.edu/flash/2015/from-corgis-to-corn-a-brief-look-at-the-long-history-of-gmo-technology/> [<https://perma.cc/HU3X-E2GG>].

4. *Id.*

5. JR Minkel, *Gene Behind Mendel's Green Pea Seeds Finally Identified*, SCIENTIFIC AMERICAN (Jan. 5, 2007), <https://www.scientificamerican.com/article/gene-behind-mendels-green/> [<https://perma.cc/4C5Z-L9M8>].

6. Gabriel Rangel, *From Corgis to Corn: A Brief Look at the Long History of GMO Technology*, HARVARD SCIENCE IN THE NEWS BLOG (Aug. 9, 2015), <http://sitn.hms.harvard.edu/flash/2015/from-corgis-to-corn-a-brief-look-at-the-long-history-of-gmo-technology/> [<https://perma.cc/HU3X-E2GG>].

7. *Id.*

8. *Id.*

9. *See Genome Editing/Genome Engineering Market Worth 6.28 Billion USD by 2022*, MARKETANDMARKETS, <http://www.marketsandmarkets.com/PressReleases/genome-editing-engineering.asp> [<https://perma.cc/MMS2-WRC6>].

nearly \$6.28 billion.<sup>10</sup> CRISPR is already the most utilized tool in the genome editing market.<sup>11</sup> As Earth's climate continues to change, and the pace of that change escalates, humanity will need to continue adapting—potentially at a much faster rate.<sup>12</sup> Thus, the economic value found in genome editing will likely continue to increase as humanity continues to use it to adapt to the changing climate on the planet.<sup>13</sup>

A legal dispute around two of the patents involving CRISPR has been at the center of news for this technology.<sup>14</sup> The first, put forth by a team at the University of California, is directed to CRISPR-Cas9 systems not restricted to any environment.<sup>15</sup> The second, put forth by a team at the Broad Institute, is directed to CRISPR-Cas9 systems in a specific cellular environment.<sup>16</sup> The legal issue is whether the second patent is rendered obvious by the first patent, and what standard should be used to make that determination.

Part II of this note will talk about the legal background of the obviousness standard, the background of the CRISPR technology, and a brief discussion about the patents and cases in the CRISPR dispute. Part III of this note will argue for a more flexible standard to be adopted by the federal circuit, as well as suggesting new factors to be considered. Part IV will conclude the argument.

## II. BACKGROUND

When two patents potentially overlap with one another, the United States Patent and Trademark Office must resolve any issues and determine which patent gets priority.<sup>17</sup> Prior to the adoption of the America Invents Act in 2011 (“AIA”), this was done by 35 U.S.C. §

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10. *Id.*

11. *Id.*

12. Juliet Eilperin, Brady Dennis and Chris Mooney, *Trump administration sees a 7-degree rise in global temperatures by 2100*, THE WASHINGTON POST (Sept. 28, 2018), [https://www.washingtonpost.com/national/health-science/trump-administration-sees-a-7-degree-rise-in-global-temperatures-by-2100/2018/09/27/b9c6fada-bb45-11e8-bdc0-90f81cc58c5d\\_story.html?noredirect=on&utm\\_term=.f51cd1eb0d71](https://www.washingtonpost.com/national/health-science/trump-administration-sees-a-7-degree-rise-in-global-temperatures-by-2100/2018/09/27/b9c6fada-bb45-11e8-bdc0-90f81cc58c5d_story.html?noredirect=on&utm_term=.f51cd1eb0d71) (The world temperature is estimated to increase seven degrees Fahrenheit by the end of the century.) [<https://perma.cc/GS5W-QT2T>].

13. See *Genome Editing/Genome Engineering Market Worth 6.28 Billion USD by 2022*, MARKETSandMARKETS, <http://www.marketsandmarkets.com/PressReleases/genome-editing-engineering.asp> [<https://perma.cc/MMS2-WRC6>].

14. Jon Cohen, *How the battle lines over CRISPR were drawn*, SCIENCE (Feb. 15, 2017), <https://www.sciencemag.org/news/2017/02/how-battle-lines-over-crispr-were-drawn> [<https://perma.cc/396J-ZBHM>].

15. U.S. Patent App. No. 20140068797 (filed Mar. 15, 2013).

16. U.S. Patent No. 8,697,359 (filed Oct. 13, 2013).

17. 35 U.S.C. § 102.

102(g) interference proceedings.<sup>18</sup> After the AIA changes came into effect, the issues are resolved through two mechanisms known as *Inter Partes Review*<sup>19</sup> and Post Grant Review.<sup>20</sup> The pre-AIA statute for 35 U.S.C. § 102(g) will apply in this case because the AIA changes went into effect in waves and do not apply to these patents in the determination of priority.<sup>21</sup> In Section A, the nonobvious requirement for obtaining a patent will be analyzed—diving into the *Graham* analysis and the obvious-to-try standard. Section B will look at the standard of review for obviousness determination and the reasonable expectation standard. Section C will explain the biology and importance of the CRISPR/Cas9 technology and the competing patents. Section D will give a brief overview of the Patent Trial and Appeal Board’s decision and reasoning in *The Broad Institute, Inc. v. The Regents of the University of California*. Section E will give an overview of the Federal Circuit’s reasoning and decision in *Regents of the University of California v. Broad Institute, Inc.*

#### A. The Nonobvious Requirement of Patentability

The United States Constitution gives Congress the power to enact laws concerning patents.<sup>22</sup> The primary requirements of a patentable invention are utility,<sup>23</sup> novelty,<sup>24</sup> and nonobviousness.<sup>25</sup> To satisfy the utility requirement, a patent must show that it is useful.<sup>26</sup> An invention fails the novelty requirement, or is “anticipated,” when each claim of the patent is described in a single prior art reference.<sup>27</sup>

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18. 35 U.S.C.S. § 102(g) (LexisNexis 2010).

19. 35 U.S.C. § 311.

20. 35 U.S.C. § 321.

21. See *The Broad Institute, Inc. v. The Regents of the University of California*, No. 106,048 (P.T.A.B. 2017).

22. U.S. CONST. art. I, § 8, cl. 8 grants Congress the power to “promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”

23. 35 U.S.C. § 101 requires that the invention be a new and useful process, machine, manufacture, or composition of matter.

24. 35 U.S.C. § 102 requires that the invention be novel and sets out various exceptions to prior art and bars to patentability.

25. 35 U.S.C. § 103 states that a patent may not be obtained if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains.

26. See *Brenner v. Manson*, 383 U.S. 519, 535 (1966). One can fail the utility requirement when it is not apparent why the invention is useful or if the utility is not credible.

27. See *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631 (Fed. Cir. 1987). Examples of prior art under the Pre-AIA include, but are not limited to, printed publications, patents, and patent applications. 35 U.S.C. § 102.

The nonobvious requirement can trace its origins in the United States in the 1851 Supreme Court case *Hotchkiss v. Greenwood*.<sup>28</sup> The requirement was then codified in the Patent Act of 1952.<sup>29</sup> The Supreme Court tackled the language of the newly codified nonobviousness requirement in the pinnacle case *Graham v. John Deere Co. of Kansas City*.<sup>30</sup> The Court held that under 35 U.S.C. § 103, “the prior art’s scope and content should be determined, the differences between the prior art and the claims should be identified, and the level of ordinary skill in the art should resolved.”<sup>31</sup> Additionally, secondary considerations should be relevant as indicia of obviousness or nonobviousness.<sup>32</sup> The *Graham* Court listed commercial success, long-felt need, and failure of others as examples of these secondary considerations.<sup>33</sup> The *Graham* Court then cited a law review note that listed additional factors such as commercial acquiescence, simultaneous solution, professional approval, and progress through the Patent Office.<sup>34</sup> Other secondary factors weighed by the *Graham* Court include: copying by others in the field, respect by the industry, acclaim, unexpected results, skepticism, teaching away, long experimentation, and utility.<sup>35</sup> The Court of Appeals for the Federal Circuit, in an effort to apply the *Graham* analysis, used an approach known as the “teaching, suggestion, or motivation” test (“TSM test”).<sup>36</sup> In the TSM test, a patent claim is obvious only if “some motivation or suggestion to combine the prior art teachings” can be found in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art.<sup>37</sup> The Supreme Court, in *KSR Int’l Co. v. Teleflex Inc.*, overturned the TSM test.<sup>38</sup> They reasoned that “when a court transforms the general principle into a rigid rule that limits the obviousness inquiry . . . it

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28. *Hotchkiss v. Greenwood*, 52 U.S. 248, 267 (1851) (More ingenuity and skill needed than possessed by an ordinary mechanic, otherwise the invention is just the work of the skillful mechanic, not of an inventor.).

29. 35 U.S.C. § 103 (1952).

30. *Graham v. John Deere Co.*, 383 U.S. 1 (1966).

31. *Id.* at 17.

32. *Id.* at 18.

33. *Id.* at 17.

34. Jonathan J. Darrow, *Secondary Considerations: A Structured Framework for Patent Analysis*, 74 Alb. L. Rev. 47, 50 (2010) (citing Richard L. Robbins, Note, *Subtests of “Nonobviousness”: A Nontechnical Approach to Patent Validity*, 112 U. PA. L. REV. 1169 (1964)).

35. Jonathan J. Darrow, *Secondary Considerations: A Structured Framework for Patent Analysis*, 74 Alb. L. Rev. 47, 51 (2010).

36. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 407 (2007); see *ACS Hosp. Sys. v. Montefiore Hosp.*, 732 F.2d 1572, 1577 (Fed. Cir. 1984).

37. *Id.*

38. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 407 (2007).

errs.”<sup>39</sup> The *KSR* Court also stated that the fact a combination was obvious to try, when considering market pressure and the finite number of identified, predictable solutions, may be enough to show obviousness under 35 U.S.C. § 103.<sup>40</sup> The *KSR* Court reasoned that granting protection to advances that occur without real innovation slows progress and may deprive previous patents of their value.<sup>41</sup>

By overturning the TSM test and commenting on the validity of an obvious-to-try standard, the court in *KSR* effectively increased the relevance of secondary consideration and simultaneously criticized the static approaches by the Federal Circuit.<sup>42</sup> These secondary considerations may be particularly useful when expert opinions are contradictory due to the complicated nature of the invention.<sup>43</sup> Subsequent cases have seen the Federal Circuit interpret the *KSR* standard.<sup>44</sup> In *Abbot Labs v. Sandoz Inc.*, the court reasoned that *KSR*'s obvious-to-try standard should be considered in the particular context of the case. Elements of each case must be analyzed, including the characteristics of the technology, the advanced nature of the science, the specificity of the prior art, and the predictability of results in the technological field of interest.<sup>45</sup> Indeed, every case involving a question of nonobviousness should be decided upon its own facts.<sup>46</sup> The Federal Circuit also refused to limit the *KSR* holding to predictable arts, opting to include less predictable arts such as biotechnology.<sup>47</sup> However, when prior art steers a person having ordinary skill in the art away from a prior art reference, the invention cannot be deemed “obvious to try.”<sup>48</sup> The court in *Pharmastem Therapeutics, Inc. v. Viacell, Inc.* reasoned that scientific confirmation may be a valuable contribution, but it does not make an invention patentable.<sup>49</sup>

The obvious-to-try standard mentioned in *KSR* seems to be utilized when a court cannot find sufficient evidence of secondary considerations and determines nonobviousness based only on the reasoning that the invention would have been obvious for a person

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39. *Id.* at 419.

40. *Id.* at 421.

41. *Id.* at 419.

42. Jonathan J. Darrow, *Secondary Considerations: A Structured Framework for Patent Analysis*, 74 *Alb. L. Rev.* 47, 54 (2010).

43. *Id.* at 67.

44. *See Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341 (Fed. Cir. 2008).

45. *Id.* at 1352.

46. *In re Jones*, 958 F.2d 347, 350 (Fed. Cir. 1992).

47. *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009).

48. *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1359 (Fed. Cir. 2007).

49. 491 F.3d 1342, 1363-64 (Fed. Cir. 2007).

having ordinary skill in the art to try and make.<sup>50</sup> The obvious-to-try standard was originally employed prior to the adoption of the statutory nonobviousness standard.<sup>51</sup> However, prior to *KSR*, the Federal Circuit rejected the obvious-to-try standard in *In re O'Farrell*.<sup>52</sup> The *O'Farrell* court clarifies that courts generally misapply the standard.<sup>53</sup> One such misapplication is when “what was ‘obvious to try’ was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.”<sup>54</sup> The *O'Farrell* court eventually held that “[f]or obviousness under § 103, all that is required is a reasonable expectation of success.”<sup>55</sup> Post-*KSR*, the Federal Circuit has begun to side step the obvious-to-try standard by using the reasonable expectation standard.<sup>56</sup> An issue arises in scientific research, where the inherent unpredictable nature of the research clouds the correct application of the reasonable expectation of success standard.<sup>57</sup> The standard is problematic because there is not a test to determine what degree of expectation of success is “reasonable.”<sup>58</sup> Confusion has resulted as courts utilize the standard in an effort to ignore the importance of inherent unpredictability.<sup>59</sup>

To satisfy the reasonable expectation of success standard, an inventor must do more than just vary all parameters until one avenue results in success when the prior art gave no indication of either the critical parameters or the direction as to which one of the parameters is likely to be successful.<sup>60</sup> Reasonable expectation of success cannot be fulfilled by an opinion that success is inherent.<sup>61</sup> Additionally, when an inventor proceeds in opposition to accepted wisdom in their

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50. Andrew V. Trask, *Obvious to Try: A Proper Patentability Standard in the Pharmaceutical Arts*, 76 *Fordham L. Rev.* 2625, 2634 (2008).

51. See *In re Kepler*, 30 C.C.P.A. 726, 730 (U.S. C.C.P.A. 1942) (A patent should not be granted for [the] discovery of a result that would flow naturally from the teachings of the prior art.).

52. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

53. *Id.*

54. *Id.*

55. *Id.* at 905.

56. Andrew V. Trask, *Obvious to Try: A Proper Patentability Standard in the Pharmaceutical Arts*, 76 *Fordham L. Rev.* 2625, 2654 (2008); see *Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342 (Fed. Cir. 2007); see *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293 (Fed. Cir. 2007).

57. Kathleen N. McKereghan, *The Nonobviousness of Inventions: In Search of a Functional Standard*, 66 *WASH. L. REV.* 1061, 1072 (1991).

58. *Id.* at 1076.

59. *Id.*

60. *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006).

61. *In re Rinehart*, 531 F.2d 1048, 1054 (C.C.P.A. 1976).

field, that is evidence of nonobviousness.<sup>62</sup> The Federal Circuit considers reasonable expectation of success a question of fact.<sup>63</sup> The reasonable expectation of success standard seems to have originated from the 1961 Court of Customs and Patent Appeals<sup>64</sup> case, *In re Moreton*.<sup>65</sup> The court in *In re Moreton* reasoned:

What this amounts to is an argument that if one slavishly following the prior art, albeit with a little educated imagination, will sometimes succeed and sometimes fail, then he is always entitled to a patent in case of success. This is not the intention behind 35 U.S.C. 103. Obviousness does not require absolute predictability . . . the mere possibility of failure does not render their successful use “unobvious.”<sup>66</sup>

Subsequent courts ignored the statement that “the mere possibility of failure does not render their successful use ‘unobvious,’” and focused instead on the idea that obviousness does not require absolute predictability.<sup>67</sup> Building on that, the court took this notion one step further by holding that “an invention can be said to be obvious if one ordinarily skilled in the art would consider that it was logical to anticipate with a high degree of probability that a trial of it would be successful.”<sup>68</sup> A “high degree of probability” further evolved into “at least some predictability is required.”<sup>69</sup> Finally, the reasonable expectation of success standard appeared in *In re Rinehart*.<sup>70</sup>

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62. *Charles v. Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1986).

63. *Par Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1196 (Fed. Cir. 2014).

64. The Court of Customs and Patent Appeals had jurisdiction over cases regarding appeals from the Patent Office in patent and trademark cases from 1909-1982, upon which the Court of Customs and Patent Appeals was merged with the Court of Claims to form the jurisdictional basis for the Federal Circuit. See Federal Judicial Center, *U.S. Court of Customs and Patent Appeals, 1929-1982*, FEDERAL JUDICIAL CENTER, <https://www.fjc.gov/history/courts/u.s.-court-customs-and-patent-appeals-1929-1982> [https://perma.cc/HW75-DTXE]; Federal Judicial Center, *Court of Claims, 1855-1982*, FEDERAL JUDICIAL CENTER, <https://www.fjc.gov/history/courts/court-claims-1855-1982> [https://perma.cc/6VTD-8ELC]; Federal Judicial Center, *Federal Judicial Circuits: Federal Circuit*, FEDERAL JUDICIAL CENTER, <https://www.fjc.gov/history/administration/federal-judicial-circuits-federal-circuit> [https://perma.cc/DV5N-G7LF].

65. *In re Moreton*, 288 F.2d 940 (C.C.P.A. 1961).

66. *Id.* at 943-944.

67. *In re Huellmantel*, 324 F.2d 998, 1000 (C.C.P.A. 1963).

68. *In re Pantzer*, 341 F.2d 121 (C.C.P.A. 1965).

69. *In re Naylor*, 369 F.2d 765, 768 (C.C.P.A. 1966).

70. *In re Rinehart*, 531 F.2d 1048, 1054 (C.C.P.A. 1976).

### B. Standard of Review for Obviousness

Obviousness is a question of law based on underlying facts.<sup>71</sup> The underlying factual findings include the *Graham* analysis as discussed above.<sup>72</sup> Objective considerations of obviousness are questions of fact that should be reviewed for substantial evidence supporting the findings.<sup>73</sup> Relevant evidence such as secondary considerations should not be disregarded when determining obviousness.<sup>74</sup> For example, the Federal Circuit in *In Re Dow Chemical Co.* stated that the criteria for determination of obviousness is whether prior art would suggest to a person having reasonable skill in the art that “this process should be carried out and would have a reasonable likelihood of success, viewed in light of the prior art.”<sup>75</sup> Similarly, the Supreme Court in *Pfizer, Inc. v. Apotex, Inc.* held that “obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success.”<sup>76</sup> Substantial weight may be given to evidence of the unexpected nature of results in favor of nonobviousness.<sup>77</sup> Furthermore, if the evidence of a case supports several reasonable conclusions that contradict each other, the USPTO’s decision will not be found as unsupported by substantial evidence because they chose one conclusion over another alternative conclusion.<sup>78</sup> Patent laws should not have limitations and conditions read into them which the legislature has not expressed.<sup>79</sup> When prior art discloses the general conditions of a claim, one may not simply discover workable ranges by routine experimentation and call it inventive.<sup>80</sup>

### C. The CRISPR Technology.

Deoxyribonucleic acid (“DNA”), is the blueprint for life on this

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71. *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1326 (Fed. Cir. 2016).

72. *Graham v. John Deere Co.*, 383 U.S. 1,17 (1966). *See also* *Icon Health & Fitness, Inc. v. Strava, Inc.*, 849 F.3d 1034, 1039 (Fed. Cir. 2017).

73. *Arctic Cat Inc. v. Bombardier Rec. Prods.*, 876 F.3d 1350, 1358 (Fed. Cir. 2017).

74. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983) (The relevant evidence on the obviousness-nonobviousness issue ... includes evidence on what has now been called “secondary considerations.” It is error to exclude that evidence from consideration.).

75. *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988).

76. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007).

77. *Burlington Indus. v. Quigg*, 822 F.2d 1581, 1584 (Fed. Cir. 1987).

78. *In re Jolley*, 308 F.3d 1317, 1320 (Fed. Cir. 2002).

79. *Diamond v. Diehr*, 450 U.S. 175, 182 (1981) (citing *Diamond v. Chakrabarty*, 447 U.S. 303, 308 (1980)).

80. *In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955).

planet.<sup>81</sup> DNA is made up of two strands of chemical compounds called nucleotides that bind one another in complementary pairs.<sup>82</sup> This complementarity allows DNA to store an enormous amount of information in the sequence of its nucleotides.<sup>83</sup> Some of the information organized in DNA are called genes.<sup>84</sup> The entirety of an organism's DNA is referred to as a genome.<sup>85</sup> An organism's cell transcribes genes in the form of messenger ribonucleic acid ("mRNA"), and sends this "message" to machinery within the cell to produce proteins from the initial blueprint.<sup>86</sup> Proteins then carry out the functions of the organism.<sup>87</sup> When something is wrong with these proteins, they may not function correctly—potentially leading to disease.<sup>88</sup>

In many diseases, proteins function incorrectly due to errors in the DNA "blueprint."<sup>89</sup> The symptoms of these diseases lead researchers to study what protein is functioning incorrectly, and which gene encodes that protein.<sup>90</sup> These diseases can then be studied in cell lines and animals if the expression of these genes are lowered or eliminated.<sup>91</sup> The ability to edit genes is an incredibly powerful tool for both research and treatment of diseases.<sup>92</sup>

In the past few decades, tools have been developed to allow for genome editing.<sup>93</sup> The primary examples of these tools are zinc finger nucleases ("ZFNs") and TAL effector nucleases ("TALENs").<sup>94</sup> ZFNs and TALENs use custom engineered proteins to bind a specific sequence of DNA and cut the DNA in a specific spot.<sup>95</sup> Custom engineering these proteins is difficult and time

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81. JAMES D. WATSON ET AL., *MOLECULAR BIOLOGY OF THE GENE*, 21, (Beth Wilbur et al. eds.), 7th ed., 2014.

82. *Id.* at 24.

83. *Id.* at 30.

84. *Id.* at 31.

85. *Id.* at 40.

86. *Id.* at 35-36.

87. DANIEL L. HARTL & MARYELLEN RUVOLO, *GENETICS: ANALYSIS OF GENES AND GENOMES*, 14-15, (Ty Field et al. eds.), 8th ed., 2012.

88. *Id.*

89. *Id.*

90. *Id.*

91. JAMES D. WATSON ET AL., *MOLECULAR BIOLOGY OF THE GENE*, 797, (Beth Wilbur et al. eds.), 7th ed., 2014.

92. *Id.* at 797-98; If a gene is edited such that it can't be transcribed, then no protein can be made. If no protein is made, then an organism may have symptoms similar to a disease.

93. Jennifer A. Doudna & Emmanuelle Charpentier, *The new frontier of genome engineering with CRISPR-Cas9*, 346 *SCIENCE* 1077 (2014).

94. *Id.*

95. *Id.*

consuming.<sup>96</sup> The invention at issue in the patents controlled by the University of California and the Broad Institute involves a new technology, known as CRISPR-Cas9.<sup>97</sup> CRISPR is composed of a protein (Cas9) that cuts DNA, and a RNA that guides the protein to a specific site in the genome.<sup>98</sup>

To put this in an analogy, imagine there is an attorney that travels a lot for work. The attorney does not always go to the same place; in fact, they travel all over the world. Unfortunately, the attorney cannot fly, so they have to drive to all of their destinations. Suppose that the destinations represent a location within an organism's genome, and the attorney's car represents the ZFNs/TALENs or CRISPR. With ZFNs and TALENs, every time the attorney wants to go someplace new, they will have to build a new car because the directions to their destination are built into the car. With CRISPR, the car stays the same, all the attorney needs to do is download new directions. Furthermore, while in the ZFN/TALEN car, the attorney can only go to one destination; as opposed to the CRISPR car, where the attorney can go to multiple destinations in the same trip by "downloading" multiple sets of directions.

This analogy emphasizes both the flexibility and utility of the CRISPR invention. The guide RNAs which guide the CRISPR protein complex to a specific site in the genome cost around \$100 USD to create, which is very cost efficient by scientific standards.<sup>99</sup> The utility of CRISPR stretch across a wide range of industries, with the two most important being biotechnology and medical research.<sup>100</sup> Therefore, a patent that gives the right to use or license CRISPR is valuable to hold.

## 1. The University of California Berkeley Discovery and Patent

On August 17, 2012, Jennifer Doudna and Emmanuelle

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96. *Id.*

97. See *The Broad Institute, Inc. v. The Regents of the University of California*, No. 106,048 (P.T.A.B. 2017); *Regents of the University of California v. Broad Institute, Inc.*, 2018 U.S. App. LEXIS 25535 (Fed. Cir. 2018); U.S. Patent No. (filed Oct. 13, 2013); U.S. Patent App. No. 20140068797 (filed Mar. 15, 2013).

98. Jennifer A. Doudna & Emmanuelle Charpentier, *The new frontier of genome engineering with CRISPR-Cas9*, 346 SCIENCE 1077 (2014).

99. Annie Snead, *Mail-Order CRISPR Kits Allow Absolutely Anyone to Hack DNA*, SCIENTIFIC AMERICAN Nov. 2, 2017, <https://www.scientificamerican.com/article/mail-order-crispr-kits-allow-absolutely-anyone-to-hack-dna/> [https://perma.cc/BE33-CXNP].

100. Katrina Megget, *Money from Genes: CRISPR Goes Commercial*, SCIENTIFIC AMERICAN, (Jan. 22, 2016), <https://www.scientificamerican.com/article/money-from-genes-crispr-goes-commercial/> [https://perma.cc/4CH5-EFPK].

Charpentier (collectively “the University of California’s team”)<sup>101</sup> published their research paper in *Science* describing their use of the CRISPR system.<sup>102</sup> In the paper, they demonstrated the ability of CRISPR to cleave double stranded DNA for the first time.<sup>103</sup> They concluded their paper with the following statement:

Zinc-finger nucleases and [TALEN]s have attracted considerable interest as artificial enzymes engineered to manipulate genomes. We propose an alternative methodology based on RNA-programmed Cas9 that could offer considerable potential for gene-targeting and genome-editing applications.<sup>104</sup>

Even though the paper does not show CRISPR activity in a cellular environment, it does explicitly lay out the potential impact of the technology on the genome-editing field.<sup>105</sup>

In the patent application 13/842,859, filed on March 15, 2013, the relevant claim that the University of California’s team makes is Claim 165, which states:

A method of cleaving a nucleic acid comprising contacting a target DNA molecule having a target sequence with an engineered and/or non-naturally-occurring Type II Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-CRISPR association (Cas)(CRISPR-Cas) system comprising

- a) A Cas9 protein; and
- b) A single molecule DNA-targeting RNA comprising
  - i) A targeter-RNA that hybridizes with the target sequence, and
  - ii) An activator-RNA that hybridizes with the targeter-RNA to form a double-stranded RNA duplex of a protein-binding segment,

wherein the activator-RNA and the targeter-RNA are covalently linked to one another with intervening nucleotides, wherein the single molecule DNA-targeting RNA forms a complex with the Cas9 protein, whereby the single molecule DNA-targeting RNA targets the target sequence, and the Cas9

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101. Jennifer Doudna works for the University of California, Berkeley. Emmanuelle Charpentier works for the University of Vienna, and collaborated with Doudna.

102. Jinek et al., *A programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity*, 337 *SCIENCE* 816-821 (2012).

103. *Id.*

104. *Id.* at 820.

105. *Id.* at 816-21.

protein cleaves the target DNA molecule.<sup>106</sup>

The University of California's patent is not limited to any particular environment.<sup>107</sup> The Broad Institute makes the claim that this lack of limitation distinguishes their patent from the patent held by the University of California.

## 2. The Broad Institute's Discovery and Patent

On February 15, 2013, Feng Zhang published his research paper in *Science* demonstrating the use of the CRISPR system in mammalian cell lines.<sup>108</sup> This paper cited to the 2012 paper described *supra* by Doudna and Charpentier.<sup>109</sup> In the 8,697,359 patent, which was filed October 15, 2013, the Broad Institute (who employees Zhang) made the following claim:

A method of altering expression of at least one gene product comprising introducing into a eukaryotic cell containing and expressing a DNA molecule having a target sequence and encoding the gene product an engineered, non-naturally occurring Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)--CRISPR associated (Cas) (CRISPR-Cas) system comprising one or more vectors comprising:

- a) a first regulatory element operable in a eukaryotic cell operably linked to at least one nucleotide sequence encoding a CRISPR-Cas system guide RNA that hybridizes with the target sequence, and
- b) a second regulatory element operable in a eukaryotic cell operably linked to a nucleotide sequence encoding a Type-II Cas9 protein,

wherein components (a) and (b) are located on same or different vectors of the system, whereby the guide RNA targets the target sequence and the Cas9 protein cleaves the DNA molecule, whereby expression of the at least one gene product is altered; and, wherein the Cas9 protein and the guide RNA do not naturally occur together.<sup>110</sup>

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106. The Broad Institute, Inc. v. The Regents of the University of California, No. 106,048 (P.T.A.B. 2017).

107. *Id.*

108. Cong et al., *Multiplex Genome Engineering Using CRISPR/Cas Systems*, 339 SCIENCE 819-23 (2013).

109. *Id.*

110. The Broad Institute, Inc. v. The Regents of the University of California, No. 106,048 (P.T.A.B. 2017).

It should be noted that this patent was granted an accelerated examination.<sup>111</sup> In essence, the difference between this patent and University of California's application was that Broad Institute's claims were limited to the method being used in eukaryotic cells.<sup>112</sup> Regardless, the Broad Institute has attempted to create a licensing pool for the CRISPR technology, which combines other patents so that costs can be reduced and scientists may benefit.<sup>113</sup>

#### *D. PTAB Decision*

The battle over CRISPR has occurred in courts and among the researcher's scientific peers.<sup>114</sup> Major awards in the life sciences have been given to both parties for their work on CRISPR.<sup>115</sup> The University of California suggested the interference proceeding to determine if there was overlap between the two patents.<sup>116</sup> When patentably indistinct subject matter gives rise to a dispute, only the first inventor may be awarded a patent under pre-AIA 35 U.S.C. § 102(g).<sup>117</sup> The Patent Trial and Appeal Board ("PTAB") is the entity that oversees the interference proceedings.<sup>118</sup> Here, PTAB reasoned that to declare an interference, a two way test must be used in which "the subject matter of a claim of one party would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the

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111. James W. Sanner, *The Struggle for CRISPR: A Billion Dollar Question in Intellectual Property*, 2016 U. ILL. J.L. TECH. & POL'Y 431, 438 (2016).

112. *The Broad Institute, Inc. v. The Regents of the University of California*, No. 106,048 (P.T.A.B. 2017).

113. Sophie Lawrence et al., *The competition law issues of the CRISPR patent pool*, BRISTOWS CLIPBOARD (Feb. 16, 2018), <http://www.bristowscleanup.com/post/the-competition-law-issues-of-the-crispr-patent-pool#page=1> ("Having the Broad Institute on board is a promising start, but UC Berkeley, holding the patent to the underlying technology, must also join for the pool to be commercially successful.") [<https://perma.cc/Y455-A6V9>].

114. See Aaron Dy, *When will CRISPR get a Nobel Prize?*, PUBLIC LIBRARY OF SCIENCE (Oct. 5, 2017), <https://blogs.plos.org/synbio/2017/10/05/when-will-crispr-get-a-nobel-prize/> [<https://perma.cc/46QY-WXNH>]; <http://kavliprize.org/prizes-and-laureates/prizes/2018-kavli-prize-nanoscience> [<https://perma.cc/MV8P-9KDT>]; Sharon Begley, *Who gets credit for CRISPR? Prestigious award singles out three, and leaves out a notable scientist*, STAT (May 31, 2018), <https://www.statnews.com/2018/05/31/crispr-scientists-kavli-prize-nanoscience/> [<https://perma.cc/MNA9-3758>]; Kelly Servick, *Broad Institute takes a hit in European CRISPR patent struggle*, SCIENCE (Jan. 18, 2018), <http://www.sciencemag.org/news/2018/01/broad-institute-takes-hit-european-crispr-patent-struggle> [<https://perma.cc/G86M-9N87>].

115. *Id.*

116. *The Broad Institute, Inc. v. The Regents of the University of California*, No. 106,048 (P.T.A.B. 2017).

117. *Id.* at 8.

118. 35 U.S.C. § 135.

opposing party and vice versa.”<sup>119</sup> Anticipation requires that each element of a claim is found in a single reference.<sup>120</sup> The University of California admits that under this standard, none of its claims anticipate the Broad Institute’s claims.<sup>121</sup> Thus, PTAB reasoned that the Broad Institute needed to show by preponderance of the evidence that the University of California’s claims would not make the Broad Institute’s claims obvious.<sup>122</sup>

To determine obviousness, PTAB utilized the reasonable expectation of success standard described above.<sup>123</sup> The Broad Institute argued that a person having reasonable skill in the art would not have had a reasonable expectation that the CRISPR-Cas9 system would work successfully in a eukaryotic cell.<sup>124</sup> The Broad Institute used statements by the University of California inventors and their expert witness to demonstrate that a person having ordinary skill in the art lacked a reasonable expectation of success.<sup>125</sup> The University of California argues that the statements were not showing a lack of reasonable expectation of success, but rather pointing out that experimental results had not yet been reported.<sup>126</sup>

The Broad Institute also argued that the University of California’s expert witness expressed many questions demonstrating lack of reasonable expectation of success.<sup>127</sup> The University of California argues that statements clearly recognized the obviousness of using the system in eukaryotic cells and expected it would be done eventually. Their concerns were “expressing thoughts about what - if the CRISPR-Cas system did not work in eukaryotic cells, what might be the - the reasons.”<sup>128</sup> PTAB agreed with the Broad Institute’s assertion that the statements by the University of California’s inventors and expert witnesses did not demonstrate a reasonable expectation of success.<sup>129</sup> The University of California pointed to the 2012 paper predicting the potential of the system for genome editing

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119. *The Broad Institute, Inc. v. The Regents of the University of California*, No. 106,048 (P.T.A.B. 2017); *see also* *Eli Lilly & Co. v. Bd. of Regents of Univ. of Wash.*, 334 F.3d 1264, 1270 (Fed. Circ. 2003).

120. *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 999 (Fed. Circ. 2006).

121. *The Broad Institute, Inc. v. The Regents of the University of California*, No. 106,048 (P.T.A.B. 2017).

122. *Id.* at 12.

123. *Id.*

124. *Id.* at 13.

125. *Id.* at 13-15, 16-19.

126. *Id.* at 16.

127. *Id.* at 18.

128. *Id.* at 19.

129. *Id.* at 17, 19.

as support of its position.<sup>130</sup> PTAB disagreed and reasoned that the language did not indicate that the system was expected to work in eukaryotic cells.<sup>131</sup>

The next argument put forward by the University of California was the fact that many independent research groups simultaneously were able to use the CRISPR-Cas9 system in eukaryotic cells after the publication of their paper.<sup>132</sup> PTAB did not view this as a reasonable expectation of success, but rather evidence of motivation to do so.<sup>133</sup> PTAB refused to accept that a scientist's belief in success of an experiment necessarily indicates a reasonable expectation of success.<sup>134</sup> PTAB further stated that if this was adopted, subject matter would always be obvious under the *KSR* framework.<sup>135</sup>

PTAB relied on *Pfizer Inc. v. Apotex, Inc.* to state that “[u]ndue dependence on mechanical application of a few maxims of law, such as ‘obvious to try,’ that have no bearing on the facts certainly invites error as decisions on obviousness must be narrowly tailored to the facts on each individual case.”<sup>136</sup> *Pfizer* was published one month before the Supreme Court published their opinion in *KSR*.<sup>137</sup>

PTAB then supported its reasonable expectation of success argument by citing to numerous cases that utilized the reasonable expectation of success standard.<sup>138</sup> PTAB looked to whether prior art would instruct persons having ordinary skill in the art how to achieve CRISPR activity in eukaryotic cells.<sup>139</sup> PTAB also looked to prior art that showed the success or failure of similar systems that could lead to a reasonable expectation of success.<sup>140</sup> The Broad Institute cited to evidence of failed attempts of similar systems that work in vitro, but do not work well in eukaryotic environments.<sup>141</sup> The University of California pointed out that this should not be indicative of a lack of reasonable expectation of success because the similar systems were shown to actually function in eukaryotic cells.<sup>142</sup> The University of

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130. *Id.* at 16.

131. *Id.* at 22.

132. *Id.* at 23.

133. *Id.*; see also: *Abbot Labs v. Sandoz, Inc.*, 544 F.3d 1341, 1352 (Fed. Cir. 2008).

134. *Id.* at 24.

135. *Id.*

136. *Id.* at 26.

137. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348 (Fed. Cir. 2007).

138. *The Broad Institute, Inc. v. The Regents of the University of California*, No. 106,048 (P.T.A.B. 2017).

139. *Id.* at 28.

140. *Id.* at 29.

141. *Id.* at 35-38.

142. *Id.* at 39.

California also pointed to ZFNs and TALENs as similar systems that work in eukaryotic cells.<sup>143</sup> The Broad Institute distinguishes ZFNs and TALENs from CRISPR by pointing out both are naturally active in eukaryotic cells despite being prokaryotic proteins.<sup>144</sup> Thus, the Broad Institute would argue that the analogy put forth by the University of California in comparing ZFNs and TALENs to CRISPR is flawed.<sup>145</sup>

The Broad Institute distinguished another protein from CRISPR by pointing out that CRISPR is larger in size and more complex.<sup>146</sup> Smaller proteins are easier to introduce into a cell than larger proteins, so the size difference is important for the likelihood of success of introducing CRISPR into a eukaryotic cell.<sup>147</sup> PTAB also decided not to consider provisional applications filed before the Broad Institute's patent because the evidence was not available to the public.<sup>148</sup> PTAB finally reasoned that the Broad Institute had shown by preponderance of the evidence that a person having ordinary skill in the art would not have a reasonable expectation of success.<sup>149</sup> Thus, the Broad Institute's patent was not invalid due to obviousness.<sup>150</sup>

#### E. FEDERAL CIRCUIT'S DECISION

The Court of Appeals for the Federal Circuit heard an appeal on the case and released their opinion on September 10, 2018.<sup>151</sup> The Federal Circuit reasoned that the standard of review of an interference proceeding concerning obviousness is the same as an obviousness review.<sup>152</sup>

The court reviewed PTAB's ultimate conclusion of obviousness de novo, and reviewed the underlying factual finds for substantial supporting evidence.<sup>153</sup> The Federal Circuit reasoned that the case was completely dependent on the substantial evidence standard.<sup>154</sup>

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143. *Id.* at 41.

144. *Id.*

145. *Id.*

146. *Id.* at 43.

147. *Id.*

148. *Id.* at 47.

149. *Id.* at 48-49.

150. *Id.*

151. *Regents of the University of California v. Broad Institute, Inc.*, 2018 U.S. App. LEXIS 25535 (Fed. Cir. 2018).

152. *Id.* at 6.

153. *Id.* at 7.

154. *Id.*

The University of California argued that PTAB “(1) improperly adopted a rigid test for obviousness that required prior art contain specific instructions, and (2) erred in dismissing evidence of simultaneous invention as irrelevant.”<sup>155</sup> Relying on the expert testimony presented to PTAB, the Federal Circuit determined that the substantial evidence supported PTAB’s finding that the success of similar systems in eukaryotic cells had been unpredictable, relying on tailoring particular conditions to the technology.<sup>156</sup>

The Federal Circuit admits that there is evidence in the record that could have supported the University of California’s position that a person having ordinary skill in the art would have had a reasonable expectation of success of CRISPR-Cas9’s activity in eukaryotic cells.<sup>157</sup> The Federal Circuit reminded the University of California that it is an appellate body that does not reweigh evidence.<sup>158</sup>

The Federal Circuit points out that simultaneous invention alone cannot show obviousness, because if it did, then any claims involved in an interference proceeding would be unpatentable for obviousness.<sup>159</sup> The Federal Circuit ultimately affirmed PTAB’s judgment.<sup>160</sup> The Federal Circuit noted the case concerned whether the claims are patentably distinct, not whether the claims are valid.<sup>161</sup>

Ultimately, the question comes down to whether the Federal Circuit utilized the correct analysis in the determination of obviousness for the Broad Institute’s patent. If the reasonable expectation of success standard was the correct analysis, then the Federal Circuit’s ruling was correct. If more weight should have been given to secondary factors articulated in *Graham*, then the Federal Circuit’s ruling is likely incorrect. Based on Supreme Court rulings on the obviousness standard, the more correct analysis of the two standards is likely to rely on the secondary factors articulated in *Graham*.

### III. DISCUSSION

The Supreme Court and the Federal Circuit disagree over the way to handle an issue of obviousness.<sup>162</sup> The Supreme Court tends to

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155. *Id.*

156. *Id.* at 14.

157. *Id.*

158. *Id.* at 15.

159. *Id.* at 19.

160. *Id.* at 22.

161. *Id.*

162. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007); *Graham v. John Deere Co.*, 383 U.S. 1 (1966).

utilize factor tests that give the court discretion based on the facts of a particular case.<sup>163</sup> The Federal Circuit has repeatedly tried to develop rigid tests in an effort to make the standard more clear for those that hold patents and those that are potentially infringing on patents.<sup>164</sup> This part explains why the Federal Circuit was too rigid in its analysis of obviousness in *Regents of the University of California v. Broad Institute, Inc.*,<sup>165</sup> what facts should be considered by the Federal Circuit, and what analysis should be used to determine obviousness going forward.

*A. The Federal Circuit's reasonable expectation of success standard is too rigid to test obviousness*

Since the Supreme Court's ruling in *KSR v. Teleflex*, the Federal Circuit has relied on the reasonable expectation of success standard a number of times to determine obviousness.<sup>166</sup> Based on the frequency and manner by which the Federal Circuit has been applying this standard, it seems that the rule has developed into one that supplants the *Graham* analysis and ignores secondary considerations.

However, in *KSR v. Teleflex*, the Supreme Court explicitly stated “[b]ut a court errs where, as here, it transforms general principle into a rigid rule limiting the obviousness inquiry.”<sup>167</sup> The Federal Circuit seems to have ignored this statement in their rigid application of the reasonable expectation of success inquiry. The secondary considerations mentioned in *Graham* were not applied to the facts at hand. In *Regents of the University of California v. Broad Institute, Inc.*, the Federal Circuit considered the *Graham* factors and the determination of a reasonable expectation of success as a question of fact that needed substantial evidence to overturn.<sup>168</sup> The Federal Circuit admitted that the issue of obviousness is a question of law,<sup>169</sup>

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163. See *Graham v. John Deere Co.*, 383 U.S. 1 (1966).

164. See *ACS Hosp. Sys. v. Montefiore Hosp.*, 732 F.2d 1572, 1577 (Fed. Cir. 1984) (“Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination.”); *In re Moreton*, 288 F.2d 940, 944 (C.C.P.A. 1961) (The origin of reasonable expectation of success standard).

165. *Regents of the University of California v. Broad Institute, Inc.*, 2018 U.S. App. LEXIS 25535 (Fed. Cir. 2018).

166. See *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348 (Fed. Cir. 2007); *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286 (Fed. Cir. 2006); *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009); *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007); *Bayer Schering Pharma A.G. v. Barr Labs., Inc.*, 575 F.3d 1341 (Fed. Cir. 2009).

167. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1734 (2007)

168. *Regents of the University of California v. Broad Institute, Inc.*, 2018 U.S. App. LEXIS 25535, at 6 (Fed. Cir. 2018).

169. *Id.*

and erred by not considering if the Patent Trial and Appeals Board used the correct analysis in their legal reasoning. The four *Graham* factors<sup>170</sup> should be considered, with a reasonable expectation of success inquiry as a secondary factor to be analyzed in the context of other facts and considerations.

*B. The Federal Circuit should have considered more factors in the case*

The analysis of the secondary factors articulated in *Graham* should have been considered in *Regents of the University of California v. Broad Institute, Inc.* The litigation at hand ultimately determines the commercial success of each patent. Many researchers wishing to utilize the CRISPR technologies have obtained licenses from both groups. The Broad Institute's attempt to create a licensing pool for the CRISPR technology has also faced scrutiny without the addition of the University of California's patent.<sup>171</sup> If anything, a consideration of commercial success seems to help the University of California's position. Next, when considering long-felt need, there was only a six-month period between the paper by the researchers associated with the University of California<sup>172</sup> and the second paper by the researchers associated with the Broad Institute.<sup>173</sup> This short period of time does not suggest that the need was long-felt. Rather, the short period of time between the two papers suggests the need was relatively novel—the opposite of a long-felt need. When considering simultaneous solution and failure of others, it should be noted that six labs accomplished CRISPR activity in eukaryotic cells shortly after the Broad Institute's team accomplished the feat.<sup>174</sup> While the Federal Circuit is correct to say some simultaneous inventions should be expected,<sup>175</sup> the fact that there were six

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170. The prior art's scope and content should be determined, the differences between the prior art and the claims should be identified, and the level of ordinary skill in the art should be resolved." Additionally, secondary considerations should be relevant as indicia of obviousness or nonobviousness.. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

171. Sophie Lawrence et al., *The competition law issues of the CRISPR patent pool*, BRISTOWS CLIPBOARD (Feb. 16, 2018), <http://www.bristowscleanup.com/post/the-competition-law-issues-of-the-crispr-patent-pool#page=1> ("Having the Broad Institute on board is a promising start, but UC Berkeley, holding the patent to the underlying technology, must also join for the pool to be commercially successful.") [<https://perma.cc/Y455-A6V9>].

172. Jinek et al., *A programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity*, 337 SCIENCE 816-21 (2012).

173. Cong et al., *Multiplex Genome Engineering Using CRISPR/Cas Systems*, 339 SCIENCE 819-23 (2013).

174. *Regents of the University of California v. Broad Institute, Inc.*, 2018 U.S. App. LEXIS 25535, at \*18-19 (Fed. Cir. 2018).

175. "Inherent in the existence of interference practice is the principle that evidence of simultaneous invention cannot alone show obviousness, otherwise any claims involved in an

simultaneous inventions by separate labs should strengthen an argument for the invention being obvious. Consideration of professional approval, respect by the industry, and acclaim also helps the argument of the University of California. Major awards in the life sciences have favored the team from the University of California—members of the team have won the 2014 Breakthrough Prize in Life Sciences, 2015 Massry Prize, 2016 Canada Gairdner International Award, 2016 Tang Prize in Biopharmaceutical Science, 2016 Warren Alpert Foundation Prize, 2017 Albany Medical Center Prize in Medicine and Biomedical Research,<sup>176</sup> and 2018 Kavli Prize in Nanoscience.<sup>177</sup> Zhang, associated with the Broad Institute, was also named on the 2016 Canada Gairdner International Award, 2016 Tang Prize in Biopharmaceutical Science, and the 2017 Albany Medical Center Prize in Medicine, and Biomedical Research. However, the only major award he received for CRISPR in the absence of members from the University of California's team has been the Lemelson-MIT award (Zhang has an appointment at MIT).<sup>178</sup> Thus far, the awards favor the University of California due to the number and prestige of the awards received by the University of California's team in comparison to the Broad Institute's team.

However, a small number of secondary factors favor the Broad Institute. The statements from members of the University of California's team leading up to the Broad Institute's publication could suggest unexpected results and skepticism, as PTAB and the Federal Circuit believed. The Broad Institute's patent also moved through the USPTO much faster, which would strengthen the Broad Institute's argument. However, the Broad Institute paid the USPTO extra fees to fast track their application.<sup>179</sup> If foreign patent applications are given any weight, the Broad Institute's position would be weakened by the European Patent Office. The European Patent Office revoked the Broad Institute's patent, which gives the University of California's team, whose patent was approved, the

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interference would be unpatentable for obviousness." *Regents of the University of California v. Broad Institute, Inc.*, 2018 U.S. App. LEXIS 25535, at \*19 (Fed. Cir. 2018).

176. Aaron Dy, *When will CRISPR get a Nobel Prize?*, PUBLIC LIBRARY OF SCIENCE (Oct. 5, 2017), <https://blogs.plos.org/synbio/2017/10/05/when-will-crispr-get-a-nobel-prize/> [<https://perma.cc/46QY-WXNH>].

177. <http://kavliprize.org/prizes-and-laureates/prizes/2018-kavli-prize-nanoscience> [<http://perma.cc/MV8P-9KDT>].

178. Sharon Begley, *Who gets credit for CRISPR? Prestigious award singles out three, and leaves out a notable scientist*, STAT (May 31, 2018), <https://www.statnews.com/2018/05/31/crispr-scientists-kavli-prize-nanoscience/> [<http://perma.cc/MNA9-3758>].

179. Jon Cohen, *How the battle lines over CRISPR were drawn*, SCIENCE (Feb. 15, 2017), <https://www.sciencemag.org/news/2017/02/how-battle-lines-over-crispr-were-drawn> [<http://perma.cc/396J-ZBHM>].

dominant position in the European market.<sup>180</sup>

*C. Incorporating the Reasonable Expectation of Success and Obvious-to-Try Standards with the Graham Factors*

Almost all cases in patent law that deal with a question of obviousness are very context specific. In situations like this, rigid rules handed down by the court are not the ideal method for distributing justice. Rather, the court should use flexible tests with factors, such as the *Graham* secondary considerations, to apply the facts of a case and use reasonable discretion to determine what the outcome should be.

The obvious-to-try and reasonable expectation of success standards should be treated as secondary factors in a *Graham* inquiry. They could be viewed as they are now, or they could be viewed in light of other secondary factors. In scenarios motivated by an exceptionally large economic incentive, an experiment may be obvious to try because the risk is worth the reward. Similarly, the reasonable expectation of success could depend on the economic incentive in the event of success. When an industry changing patent that is extremely valuable is on the other end of the tunnel, then the probability of success needed for the expectation of success to be reasonable may be fairly low. If the patent is not particularly valuable, then that probability of success should be higher in order for the expectation of success to be reasonable. In other words, reasonable expectation of success should be interpreted more as a reasonable probability of success.

Applying this standard to the CRISPR dispute, it was foreseeable that CRISPR would change billion-dollar industries, thus the reasonable likelihood of success to suggest to a person having ordinary skill in the art to try should not be very high. The rewards from a tool of this scale would outweigh the risk despite low odds.

As a policy matter, the purpose of the patent system is to grant an exclusive monopoly to a patentee in exchange for their timely disclosure of their invention so that said invention could be used for public good once the patent expires. Here, the team from the University of California filed first and their claims would seem to make the Broad Institute's claims obvious. Future inventors in the genome editing sciences could look to this case and decide not to disclose their invention until there has been proof of concept in

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180. Kelly Servick, *Broad Institute takes a hit in European CRISPR patent struggle*, SCIENCE (Jan. 18, 2018), <http://www.sciencemag.org/news/2018/01/broad-institute-takes-hit-european-crispr-patent-struggle> [http://perma.cc/G86M-9N87].

eukaryotes. This could harm the progress of the sciences, which is in direct opposition to the stated purpose of the United States Constitution in permitting Congress to grant patents.<sup>181</sup>

#### IV. CONCLUSION

In its most recent decision dealing with the obviousness standard, the Supreme Court warned against using too rigid of a test to determine whether an invention was obvious in light of the prior art. Indeed, the standard used by the Supreme Court has been a factor analysis, which gives the lower courts plenty of flexibility to rule on a case. Patent law in particular is a field of law in which disputes are context specific. Thus, the flexible secondary factor analysis used by the Supreme Court is superior to the rigid reasonable expectation of success standard utilized by the Federal Circuit.

Here, the team from the University of California were the first to patent the CRISPR invention in an unrestricted system. Multiple labs made the CRISPR system work in eukaryotes shortly after the Broad Institute. The University's researchers posited the idea of using CRISPR in eukaryotes in their publication. The economic incentive is so large that the likelihood of success does not need to be very high in order for it to be reasonable to try. The next step in the University of California's invention was to make it work in eukaryotes with standard practices, thus the Broad Institute's patent was obvious to try. Other scientists in the biological sciences seem to be awarding the University of California's researchers more than the Broad Institute's researchers. A real possibility exists that the University of California's team will win the Nobel Prize. There seems to be a disconnect between the law and the scientific community that may result in an absurd scenario in which the University of California's team could win the Nobel Prize for CRISPR without holding the most valuable patent for CRISPR, which belongs to the Broad Institute.

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181. U.S. CONST. art. I, § 8, cl. 8 grants Congress the power to "promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."