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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JOHN D. COATES

Appeal 2019-000658
Application 15/101,267
Technology Center 1600

Before SALLY GARDNER LANE, RAE LYNN P. GUEST, and
DEBORAH KATZ, *Administrative Patent Judges*.

LANE, *Administrative Patent Judge*.

DECISION ON APPEAL

I. Statement of the Case

Appellant¹ seeks review under 35 U.S.C. § 134(a) of the final rejection of claims 50–52 and 54–70 of application 15/101,267, filed June 2, 2016. (Appeal Brief filed May 23, 2018 (Appeal Br.) 2).

We have jurisdiction under 35 U.S.C. § 6(b). We REVERSE.

¹ We use the term “Appellant” to refer to the “applicant” as defined in 37 C.F.R. §1.42. Appellant identifies the real party in interest as the Regents of the University of California (Appeal Br. 1.)

II. Claims on Appeal

The claimed invention is a method of culturing a cell that has been recombinantly engineered to express chlorite dismutase in a culture medium that also contains contaminating microorganisms. The culture medium is treated with chlorite in an amount sufficient to kill the contaminating microorganisms but without killing the cultured cell. (Appeal Br. 11). The method is said to be useful in improving industrial fermentation hygiene where the cultured cell produces a fermentation product such as ethanol or butanol. (Specification filed June 2, 2016 (Spec. ¶ 6).

III. Evidence

The Examiner cited the following references in support of the rejection:

Coates, WO 2012/166964 A1, published December 06, 2012 (Coates). (Final Act. 10).

Jaime Mullerat et al., *Efficacy of Salmide, a Sodium Chlorite-Based Oxy-Halogen Disinfectant, to Inactivate Bacterial Pathogens and Extend Shelf-Life of Broiler Carcasses*, 57(7) *Journal of Food Protection* 596–603 (1994) (Mullerat). (Final Act. 12).

Brandon Goblirsch et al., *Chlorite dismutases, DyPs, and EfeB: 3 microbial heme enzyme families comprise the CDE structural superfamily*, 408(3) *Journal of Molecular Biology* 379–398 (2011) (Goblirsch). (Final Act. 11).

IV. Rejection

There is one rejection before us. Claims 50–52 and 54–70 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Coates in view

of common knowledge. (Final Act. 10).²

V. Discussion

A. Claims on Appeal

Claim 50 is representative of all the claims on appeal, claims 50–52 and 54–70, and is reproduced below:

50. A method of culturing a cell, comprising:

a) culturing a cell recombinantly engineered to express a functional chlorite dismutase in a culture medium under conditions whereby the chlorite dismutase is expressed in said cell, wherein said culture medium comprises one or more contaminating microorganisms, wherein the chlorite dismutase is expressed in the cell from a chlorite dismutase gene (*cld*) heterologous to the cell; and

b) treating said culture medium with chlorite in an amount sufficient to kill said one or more contaminating microorganisms without killing said cell, wherein the chlorite dismutase protects the cell from toxic effects of the chlorite.

(Appeal Br. 11).

According to Appellant, the claimed invention relies, in part, on the surprising discovery that a host cell, recombinantly engineered to express chlorite dismutase, is protected from the toxic effects of chlorite allowing

² The Final Action was entered February 23, 2018. The Examiner withdrew the rejection made under 35 U.S.C. § 102(a)(2). (Ans. 3).

the recombinant cell to grow even while contaminating microorganisms are killed. (Appeal Br. 5).

B. Obviousness over Coates and common knowledge

The Examiner found that Coates teaches a method of inhibiting growth of sulfate-reducing bacteria (SRB) in systems such as oil and gas pipelines. The Examiner found that Coates teaches SRB growth may be inhibited by adding chlorite and dissimilatory perchlorate-reducing bacteria (DPRB). The Examiner found that, according to Coates, the DPRB may be bacteria that naturally exhibit perchlorate reducing activity or a microorganism that is engineered to have the activity through introduction of a chlorite dismutase (*cld*) gene. (Final Act. 10–11; Examiner’s Answer of September 19, 2018 (Ans.) 5–6).

The Examiner found that Figure 1 of Coates shows that undesirable hydrogen sulfide, produced by SRB in oil reservoirs, can be controlled by either 1) neutralizing hydrogen sulfide production by adding DPRB and chlorite, which oxidizes hydrogen sulfide to non-toxic sulfur for removal, or 2) reducing the growth of, or killing, the SRB. (Ans. 7).

Figure 1 of Coates is reproduced below:

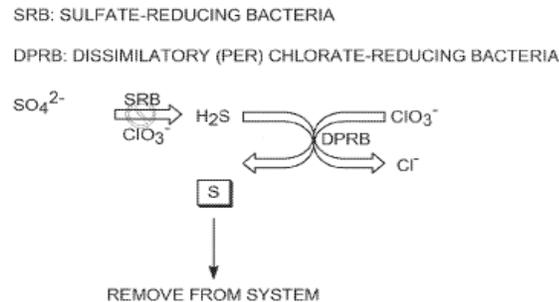


FIG. 1

Figure 1 of Coates is shown above.

The Examiner also found that Figure 5 of Coates, showing percentage inhibition of sulfidogenesis (hydrogen sulfide production), can be seen as showing cell death of the SRB where DPRB, or both DPRB and chlorate, are present. (Ans. 8, 9).

The Examiner points to Mullerat as an “evidential reference”³ to teach the efficacy of salmide, a sodium chlorite based oxyanion, as a well-known kitchen disinfectant for killing or reducing the growth of microorganisms including *Salmonella typhimurium*. The Examiner reasoned that chlorite also would be expected to kill the SRB contaminant “and that would solve the problem that had arisen in that oil and gas field.” (Ans. 7, 8).

³ Goblirsch, also relied upon by the Examiner as an evidential reference, appears only to pertain to a limitation found in dependent claim 66. (Ans. 9).

The Examiner concluded therefore that the claims would have been obvious since one of ordinary skill in the art would have been motivated to inhibit, kill or reduce the growth rate of undesirable or contaminating microorganism growth for public health and financial reasons. (Final Act. 12). The Examiner determined that one of ordinary skill in the art would have a reasonable expectation of success because Coates teaches that adding chlorate, or chlorite and perchlorate, in a culture medium allows the chlorite to kill or reduce undesirable or contaminating microorganisms or non-*cld* expressing microorganisms. (Final Act. 12).

Appellant argues that the Coates method is not directed to killing contaminating microorganisms and thus does not teach or suggest the limitation of “treating said culture medium with chlorite in an amount sufficient to kill said one or more contaminating microorganisms without killing said cell, wherein the chlorite dismutase protects the cell from toxic effects of the chlorite.” Instead, the Appellant urges that Coates shows methods of controlling the sulfide content in oil and gas reservoirs by introducing into these systems perchlorate-reducing bacteria and a chlorine oxyanion to drive the redox reaction, illustrated at Figure 1, which causes a reduction in sulfide production by the SRB. Appellant urges that, in Coates, the chloride oxyanion is added to drive a redox reaction but “does not kill anything, and the dismutase does not protect anything from chlorite toxicity.” (Appeal Br. 4, 5).

The Appellant disagrees with the Examiner’s finding that Coates teaches that “[t]he chlorine oxyanions are added at a concentration sufficient

to stimulate perchlorate-reducing activity of the microorganisms and killing cell[s] lacking chlorite dismutase.” (Appeal Br. 4 (emphasis omitted)).

Appellant asserts that there is no such statement in, or fairly inferable from, Coates. Appellant argues, “[n]owhere does [Coates] disclose or suggest that the chlorine oxyanions kill the sulfate-reducing bacteria, nor anything else: to the contrary, the redox chemistry of [Coates] is premised on the sulfate-reducing activity of the sulfate reducing bacteria, and the bacteria continue to grow just fine in cultures treated with chlorate oxyanions.” (Appeal Br. 4). Appellant argues that the Examiner has not provided a rational basis nor evidence to support the finding that the sulfate-reducing bacteria found in the Coates method were killed or even had a reduced growth rate. (Appeal Br. 4).

We agree with the Appellant that the Figure 1 reaction, relied upon in the rejection, does not expressly disclose the killing, or even reduction in growth, of SRB. Coates describes Figure 1 as showing a schematic of redox reactions occurring in a system containing SRB and DPRB in the presence of sulfate and chlorate ions. In that reaction, according to Coates, SRB reduces sulfate ions to produce hydrogen sulfide. According to Coates, the chlorate ions inhibit the formation of hydrogen sulfide by inhibiting the sulfate-reducing activity of the SRB. Coates goes on to say that, “[w]ithout wishing to be bound by theory,” it is believed that the effect is due to inhibition of sulfate uptake by the SRB, inhibition of the ATP-sulfurylase enzyme in SRB, or inhibition of the APS-reductase enzyme in SRB, or a combination of these, all required for efficient reduction of sulfate by SRB.

(Coates ¶ 22). Further, Coates indicates that the presence of chlorate ions allows DPRB to oxidize the hydrogen sulfide to elemental sulfur coupled with reduction of chlorate ions to chloride ions allowing the produced sulfur to be removed from the system. (Coates, Fig. 1; ¶ 22).

Coates does not describe the Figure 1 reaction as resulting in reduced growth or killing of the SRB. While the production of hydrogen sulfide is inhibited, Coates does not indicate that this occurs because the SRB are killed. Further, as Appellant points out, the observations illustrated at Figure 5 are not described by Coates as inhibition of growth, or killing, of the SRB. (Appeal Br. 4). Figure 5 of Coates shows “the percent inhibition of sulfidogenesis” by the SRB when incubated with DPRB and chlorate, or chlorate alone. (Coates Figure 5; ¶¶ 26, 112). Coates states that after a 24 hour incubation with DPRB and chlorate oxyanions, illustrated at Figure 5, it was observed “that thick cell growth [of the SRB] was still apparent” (Appeal Br. 8, referring to Coates ¶ 112).

Thus, the Examiner has not shown sufficient support for the finding, underlying the conclusion of obviousness, that Coates teaches that the culture medium is treated with chlorite in an amount sufficient to kill contaminating microorganisms or in an amount that would be sufficient to kill the microorganisms without killing the transformed cultured cell. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966) (The ultimate determination as to obviousness is based on underlying factual inquiries one of which is the scope and content of the prior art).

The Examiner also relied upon common knowledge that chlorite is a known disinfectant to support the rejection of the claims. The Examiner pointed to the evidential reference to Mullerat and a teaching in Coates that in pure culture chlorite can kill nitrate reducing bacteria, to further support the rejection. (Ans. 7). However, the Examiner does not articulate sufficient reasoning why, or how, one skilled in the art would have modified, with a reasonable expectation of success, the methods of Coates in a manner that would result in the killing of contaminating microorganisms without killing the transformed cultured cell, where the chlorite dismutase protects the cell from toxic effects of the chlorite. *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (“[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.”), quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

The Examiner has not shown, by the required preponderance of the evidence, that the method of claim 50 would have been obvious over the cited references and common knowledge. See *In re Epstein*, 32 F.3d 1559, 1564 (Fed. Cir. 1994) (A preponderance of the evidence is the standard for rejecting claims at the USPTO). All the other rejected claims depend from claim 50. These claims also require treating the culture medium with chlorite in an amount sufficient to kill contaminating microorganisms without killing the cultured cell having protective chlorite dismutase. Accordingly, the rejection of these claims likewise is not supported by a

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preponderance of the evidence. We therefore REVERSE the rejection of all the appealed claims.

VI. Decision

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
50-52, 54-70	103	Coates		50-52, 54-70

REVERSED