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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Wright et al.

Serial No.: 15/468,494

Filed: March 24, 2017

For: Novel Herbicide Resistance Genes

Confirmation No.: 6867

Examiner: David H. Kruse

Group Art Unit: 1663

Attorney Docket No.: 14764-262737
(63979A-US-CNT[3])

DECLARATION UNDER 37 C.F.R. § 1.132 OF DR. TERRY R. WRIGHT

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Terry R. Wright, declare:

1. I am currently a Distinguished Laureate at Corteva Agriscience (formerly Dow AgroSciences, LLC), in Indianapolis, Indiana. I am a citizen of the United States of America. I have 29 years of research experience in the fields of agronomy, pesticide

science, and plant biotechnology. I received two Bachelor of Science degrees (B.S.) in Crop and Soil Science and Agricultural Biochemistry from Michigan State University, a Master of Science (M.S.) degree in Crop Science/Weed Science from Washington State University, and a Doctorate of Philosophy (Ph.D.) from Michigan State University in Herbicide Physiology and Plant Biotechnology. I am a co-inventor on over 50 granted U.S. patents, and an author of 20 peer-reviewed scientific journal articles. My research has been in the areas of crop protection and trait discovery and development. I am an expert in the field of herbicide physiology and herbicide resistance, weed control, and trait discovery and development.

2. I am an inventor and am very familiar with the contents of the subject application, U.S. Patent Application No. 15/468,494 ("the '494 Application"). I am informed and believe that the claims currently pending in the '494 Application reflect those attached hereto as Appendix I. I have reviewed and understand those claims.
3. I understand that this Declaration will be filed in support of the patentability of the claims pending in the '494 application.
4. I understand that in the final Office Action of May 3, 2021 in the '494 Application, the U.S. Patent and Trademark Office has rejected claims 27-39, 41-54, and 57-59 of the '494 Application as being unpatentable over Kaphammer (U.S. Patent 5,608,147) in view of Schleinitz et al (September 2004, Applied and Environmental Microbiology 70(9): 5357-5365) and Pallett et al (U.S. Patent 7,205,561 B1, § 371 (c)(1) date of 15 June 1998). (Office Action at point 6).
5. I have been asked to comment on whether a person of ordinary skill in the art at the time of the invention in 2005 would have thought the transgenic plant cell, encompassed by the claims, or the use of a plant comprising such cells in a method to control weeds, was obvious in light of the prior art teachings.
6. Prior to 2005, the scientific community had recognized that the *TfdA* gene could be expressed in transgenic plants to impart 2,4-D resistance in dicot plants (e.g., cotton and tobacco) normally sensitive to 2,4-D (Streber *et al.*, 1989; Lyon *et al.*, 1989; Lyon *et al.*,

1993). Furthermore, a large number of *tfdA*-type genes that encode proteins capable of degrading 2,4-D had been identified from the environment and deposited into the Genbank database. However, although many α -ketoglutarate-dependent dioxygenases were known, no gene except *tfdA* had exhibited the ability to degrade phenoxy auxin herbicides when inserted into plant cells.

7. At the time of the invention, the standard practice used for identifying proteins exhibiting a similar functionality to a known protein was to screen for proteins having a high level of amino acid sequence identity with the known protein, and then test those selected proteins for activity. Accordingly, to identify *tfdA*-type genes that encode proteins capable of degrading 2,4-D when expressed in plants (similar to the activity of the *tfdA* gene), one would traditionally select a protein having high sequence identity with TfdA.
8. The *sdpA* gene from *Delftia acidivorans* (as disclosed in Westendorf et al., 2002, 2003 and Schleinitz et al) encodes an enzyme (SdpA) that is distantly related to TfdA. SdpA had previously been shown to degrade S-dichloroprop (Westendorf et al., 2002 and 2003) but also 2,4-D (albeit, relatively poorly) based on *in vitro* assays. More particularly, the Westendorf 2003 article (Acta Biotechnol 23:3 shows preference of S-dichloroprop over 2,4-D by >3-fold (see Table 3). Furthermore, Schleinitz et al (cited by the Examiner) states on page 5363 (first column, first full paragraph) that "SdpA shows greatest activity with the S enantiomers of mecoprop and dichloroprop but has some activity toward 2,4-D". However, the recited enzymatic activity of SdpA was limited to *in vitro* assays and SdpA was known to have low homology to TfdA (31% amino acid identity). At the time of the invention, SdpA had never been expressed in plants, nor was there any motivation to do so.
9. Those skilled in the art appreciate that there is a high level of unpredictability associated with expressing bacterial genes in plant systems. This fact is highlighted by comparing the activity of two *tfdA* homologs expressed in plants. Appendix II provides data originally presented in Example 17.1-17.5 of US Patent no 7,838,733 comparing the activity of two α -KG dioxygenase enzymes referred to as AAD-1 and AAD-2.

10. AAD-2 is more closely related (about 44%) at the sequence level to *tfdA* than is AAD-1 (about 27%). Furthermore, AAD-2 was determined to have $V_{\max}$ almost 8-fold higher than AAD-1 for 2,4-D, based on a standard *in vitro* assay. However, while, AAD-2 has a higher percentage sequence identity with *tfdA* relative to AAD-1, and in spite of AAD-2 having significantly higher *in vitro* activity for degrading 2,4-D, AAD-2 was surprisingly inactive when expressed in plants, while AAD-1 was very active.
11. In my opinion, one of ordinary skill in the art, being cognizant of the unpredictability associated with expressing bacterial genes in plant systems, would not have been motivated to specifically select a bacterial gene having low sequence identity to *tfdA* when attempting to express another gene that would provide tolerance to a phenoxy auxin herbicide. At the time of the invention there were over 100 other known *tfdA* homologs that share higher sequence identity with the *tfdA* gene than *sdpA*. Each of these homologs represent a gene that one could consider as a possible candidate for providing aryloxyalkanoate dioxygenase activity. Typically, one looking for a substitute gene would select a homolog having the highest sequence identity to the gene to be replaced, and selecting a gene having low sequence identity relative to the gene to be replaced, when other genes having higher sequence identity were available, would be acting contrary to conventional wisdom, in my opinion.
12. Although *SdpA* (AAD-12) had been identified at the time of the present invention as being capable of catalyzing a reaction analogous to that of *TfdA*, no examination of other herbicidal substrates of *SdpA* outside of the phenoxy auxin class were reported before the present invention. As a result of the present invention, it was discovered that *SdpA* render the plants resistant to one or more pyridyloxyacetate herbicides such as triclopyr and fluroxypyr. At the time of invention, no other α -KG dioxygenase enzymes had been reported to render the plants resistant to a phenoxyacetic acid herbicide (such as 2,4-D) and one or more pyridyloxyacetate herbicides such as triclopyr and fluroxypyr.
13. For the above reasons, it is evident to me, as one skilled in the art, that the combined teachings of Kaphammer in view of Schleinitz et al. and Pallett et al. fail to suggest or

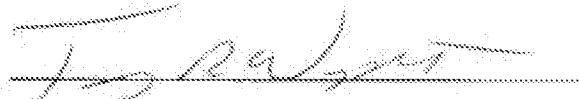
provide any guidance of how to obtain a gene and recombinant plant that has the functionality of the present claimed invention.

14. I hereby declare that all statements made herein are true and that they are based on my own knowledge, information and belief.

Place and Date: 7/29/2021

By:

Indianapolis, Indiana



Terry R. Wright

Distinguished Laureate

Corteva Agriscience