SUPPORT FOR THE MANAGEMENT OF INTELLECTUAL PROPERTY WITHIN THE PIERCE'S DISEASE RESEARCH INITIATIVE AND RESEARCH COMMUNITY

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ABSTRACT
The Public Intellectual Property Resource for Agriculture (PIPRA) and the California Department of Food and Agriculture Pierce's Disease/Sharpshooter Board (Board) began collaborations in 2005 with the goal of instituting an intellectual property (IP) management strategy inline with the Pierce's disease (PD) research consortium's mission. Within the last year, a number of information resources have been made available by PIPRA specifically tailored for the PD research community. These resources include a publicly accessible, live and comprehensive database of all PD related IP and scientific literature, an analysis of the IP and scientific literature surrounding PD research, and an IP landscape surrounding a promising PD specific technology. Collectively, these resources allow scientists to have an integrated view of the technical and legal aspects involved in their projects.

INTRODUCTION
The Public Intellectual Property Resource for Agriculture (PIPRA) is a not-for-profit research organization hosted by the University of California, Davis. PIPRA currently represents 41 public sector organizations from twelve different countries and its mission is to enable access to agricultural intellectual property (IP). PIPRA offers a range of services to address legal issues that arise during research and deployment of bio-technologies. PIPRA and the California Department of Food and Agriculture Pierce's Disease/Glassy-winged Sharpshooter Board (Board) began collaboration in 2005 to address IP issues surrounding Pierce's disease (PD) research and development. In particular, the threat PD poses to California's $16.5 billion wine industry requires foresight to seek and secure commercial deployment of feasible technologies resulting from funded research. In terms of IP, the Board would like to ensure that technologies with the potential to control PD could be promptly deployed without becoming tangled in a legal web of licenses, rights, and lawsuits.

Technologies resulting from research funded by issue-focused consortia and conducted at multiple institutions, as in the case of the PD consortium, can face three basic IP problems during research and development. First, the researchers themselves may not be aware of their obligations or opportunities with regard to patenting research discoveries. Second, once patented, new discoveries are rightfully the property of the funded research institution or university, which may have internal policies regarding licensing that may be inconsistent with the objectives of the consortia. And third, the new technologies may be blocked by already existing patented technologies. These kinds of IP issues are not uncommon in industry consortia. They are, however, often resolved up front by contractual relationships or formal joint ventures that take into account the participants' IP management strategies. Consortia of universities and other public research entities, however, typically do not have developed IP management strategies in place, in part due to the fact that public sector researchers often pay little heed to the proprietary nature of their research inputs and outputs.

PIPRA recognizes that an IP management strategy for the PD consortium needs to take a multilateral approach toward maximizing the effectiveness of the consortium's intellectual assets. Rather than focusing solely on IP protection, IP management for the PD consortia should also set milestones for technology development, assess marketing opportunities, and seek a better negotiating position during IP exchange. In essence, PIPRA seeks to aid the Board in coordinating IP to allow for access and protection, both of which are essential to the productivity of research across multiple institutions, while creating opportunities and incentives for further commercial development.

The first step toward effective IP management is the availability of information resources specifically tailored to Board funded PD researchers. Such resources provide scientists with technical and legal information critical for the deployment of marketable products with maximum security over IP rights. This report discusses the information resources specific to the PD research consortium developed by PIPRA. Included will be detailed descriptions of the IP and scientific literature database

geared towards PD specific research, an analysis of the information therein, and a biotechnology case study illustrating the types of IP issues intrinsic in emerging PD control biotechnologies.

OBJECTIVES

1. Development and maintenance of an IP and scientific literature database dedicated to PD.
2. Broad analysis of the current trend in the IP and scientific literature surrounding research in PD.
3. Analysis of the IP landscape surrounding a target technology directly related to Pierce's disease in grapes.

RESULTS

Objective 1

The IP and scientific literature database (e.g. the PD/GWSS-PIPRA database) was designed with a vision to provide state-of-the-art patent and scientific literature search and analysis tools. The PD/GWSS-PIPRA database currently contains over 6,000 IP records and over 2,500 scientific publications. This library of IP and scientific literature is updated on a quarterly basis to include the most recent IP disclosures and scientific publications available to PIPRA.

PIPRA launched an *alpha*- version of the PD/GWSS-PIPRA database in February 2006. Seventeen PD-researchers were selected to test the functionality and usability of the *alpha*-version database. The greatest concerns raised by testing researchers included slow query search speeds, the inability to connect directly to a publication of interest and the lack of a help menu. PIPRA worked with database technicians at M-CAM Inc. (http://www.m-cam.com) to resolve these issues. M-CAM optimized the searching algorithm of the PD/GWSS-PIPRA database so that search times would be cut drastically. PIPRA integrated OpenURL resolvers into the PD/GWSS-PIPRA database in order to allow researchers to directly connect to scientific publications. OpenURL resolvers are applets which can detect the end-user's host institution and connect to a publication if the institution holds a subscription to the publication. PIPRA is actively working to implement OpenURL resolvers for all institutions funded by the Board. The *beta*-version of the PD/GWSS-PIPRA database was released in May 2006. This version addresses most technical issues experienced in the *alpha*-version, including the lack of a help menu. The *beta* version (Figure 1) was also aesthetically redesigned and introduced a help menu for a more user-friendly interface. Currently, the database provides two search methods, SmartText™ and Compass™. SmartText™ allows the end-user to search across all records in the PD/GWSS-PIPRA database using a keyword or a search string. Searches can be initiated either as Boolean or advanced searches. Boolean searches allow the user to choose up to four fields to across which to search; a total of 29 fields are available. The Boolean search form also allows users to limit the returned records to patents, scientific literature, or to include both. Advanced searching is designed for generating more dynamic queries and requires that the user be familiar with creating search strings. A Compass™ search allows users to retrieve bibliographic and legal information on one or two specific patents. Compass™ also has the capability to display two patents side-by-side for easy comparison.

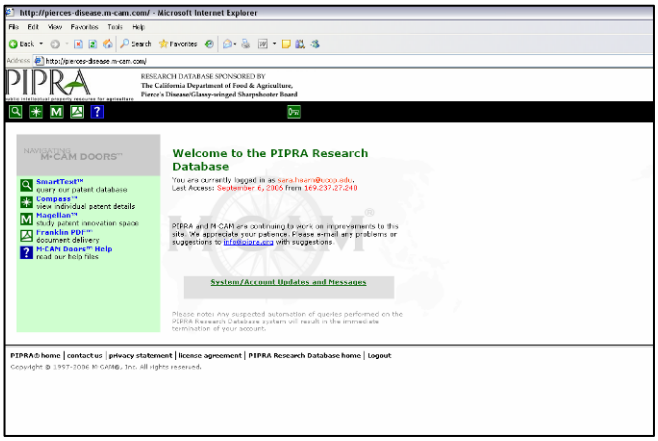

Figure 1: PD/GWSS-PIPRA database (**http://pierces-disease.m-cam.com**)

Scientists and IP professionals alike can utilize the PD/GWSS-PIPRA database prior to intiating or during PD related research. Valuable information, such as availablity of substitute technologies, with less IP restrictions, and complementary technologies, to ehance marketing opportunities, can be identified using the PD/GWSS-PIPRA database. Furthermore, because this database is commited to the field of PD, many of the IP records listed in the database will be the result of other Board funded research projects at other public sector universities, and in certain situations, be more readily licensable. Collectively, this information can help scientists conduct research to develop promising technologies with more ease of mind over its ultimate commercial viability.

Objective 2

PIPRA conducted an analysis of the scientific literature and IP surrounding PD research. The analysis has helped the Board and PIPRA better understand the magnitude of PD related research conducted across the United States. This information can be used early on to identify potential commercial partners and/or independent researchers who may be aligned with the consortium's goals. PIPRA will be using the information gathered in this analysis to launch a thorough survey on the impact the Board's funding has had on progress towards controlling PD.

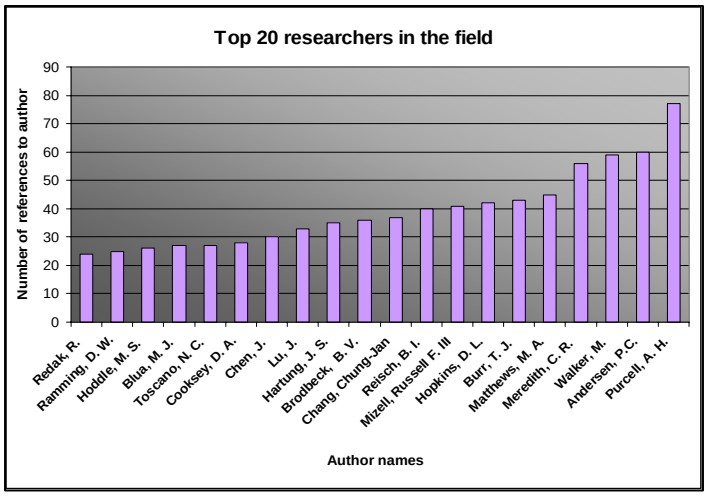

Figure 2. Top 20 Authors of PD-related publications.

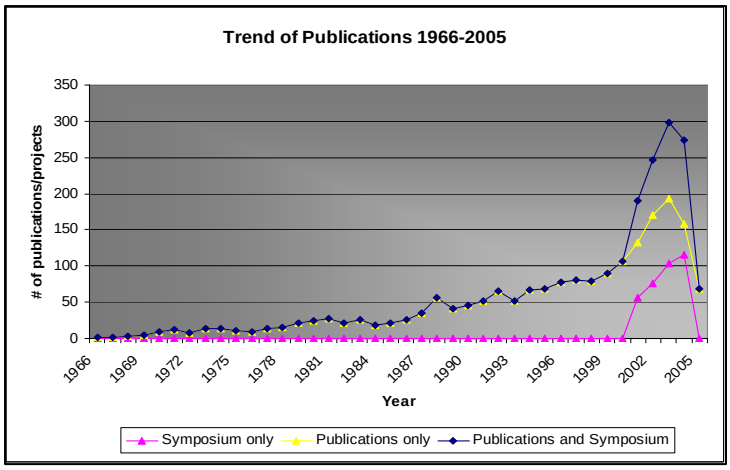

Figure 3. Number of PD-related publications per year.

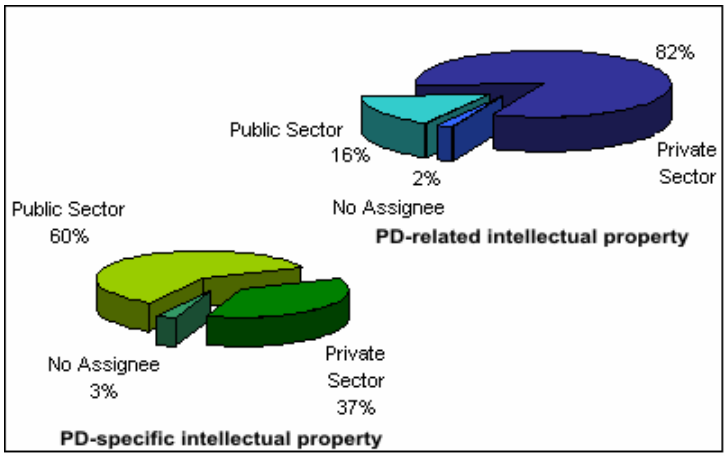

Figure 4. Distribution of IPR (patents and patent applications) in the public and private sectors.

Analysis of the scientific literature surrounding PD identified Dr. Sandy Purcell as the single most active publisher. Dr. Purcell is listed as principle investigator on over 70 publications (Figure 2). University of California, Davis and University of California, Riverside were identified as most active PD research institutions. Publishing trends in journals and symposium proceedings within the last 40 years (Figure 3) were also analyzed. A rise in the number of publications was noticeable beginning 2001. This is attributed to the increased funding PD related research received following the Board's establishment in 2001.

Analysis of the IP surrounding PD identified a total of 6,335 US patents and patent applications in the broad area of plant disease resistance but only 30 of these records described PD specific technologies. The remaining 6,305 records involved technologies applicable to *vitis*, biological control strategies and disease resistance systems. PIPRA researched the distribution of these IP rights (IPR) and found that, of the group of 30 IPR, 60 percent were owned by public sector institutions and 37 percent were owned by private industry (Figure 4). This indicated that PD-specific research was more intensive at public-sector institutions. In contrast, of the group of 6,305 broad-based IPR records, only 16 percent of the technologies were owned by public sector institutions while approximately 82 percent were owned by private industry. This distribution was not surprising since many pesticidal control systems, which were included in the 6,305 records, had been developed by chemical manufacturers in the private sector. This analysis also revealed that within the public sector, the University of Florida (Florida) had been most active in patenting PD related technologies. Collected data indicates that while only three researchers from Florida are funded by the board, the university is assignee on 42 percent of PD-related technologies within the public sector.

Objective 3

PIPRA conducted an IP analysis case study on a novel PD control technology developed by Dr. Goutam Gupta and supported by the Board. Dr. Gupta and colleagues developed an anti-microbial technology for rendering *vitis* crops resistant to PD (Dandekar 2005). A patent application (US serial no. 10/846,172) for the technology had already been filed on behalf of the inventors. For this case study, PIPRA illustrated how IP considerations, in addition to patenting, could help develop a research plan that supports commercial deployment. PIPRA researched the prior art, scientific literature, and IP landscape pertaining to a case study technology and aimed to capture IPR related to the major components and processes used by the technology.

Analysis of the IP surrounding Gupta's technology revealed a complex landscape containing many legally protected biological components. PIPRA was able to show how many of the components used by Dr. Gupta's biological construct and which required multiple licenses, could be replaced by functionally equivalent components with greater freedom-to-operate.

Moreover, the analysis also touched on the regulatory and social issues which could potentially rise during commercialization; Dr. Gupta's anti-microbial technology utilizes a human protein, a construct which is acceptable for research purposes but not desirable for a marketable ag-product. PIPRA is currently developing plant transformation enabling technologies designed to offer the possibility of incorporating, where possible, plant-derived components.

CONCLUSION

The development of a successful IP management strategy is essential to creating a strong IP portfolio. With the advent of the information resources made available by PIPRA, scientists within the PD research community are now better capable to plan research projects with proprietary values in mind. PIPRA also recognizes that these resources are only a part of a successful IP management strategy. Within the next year PIPRA will continue to build on these tools by exploring the impact Board funding has had on PD research and by conducting a thorough IP audit of a target technology in order to identify embedded IPR that could affect commercialization. These services will help implement an IP management strategy as the PD consortium prepares to advance the research and development of emerging industry solutions.

REFERENCES

Dandekar, A.M., G. Gupta, K. McDonald, E. Hong-Geller. 2005. Design of Chimeric Anti-Microbial Protein for Rapid clearance of *Xylella*, pp. 233–236. In Proceedings, 2005 Pierce's Disease Research Symposium, 5–7 December 2005, San Diego, CA.

FUNDING AGENCIES

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EXPLOITING *XYLELLA FASTIDIOSA* PROTEINS FOR PIERCE'S DISEASE CONTROL

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ABSTRACT

The aim of this project is to construct and express in test plants, and then in grapevine, a protein or protein chimera ("anti-*Xf* protein") capable of inactivating or otherwise interfering with the infectivity of *Xylella fastidiosa* (*Xf*), the causative agent of Pierce's disease of grapevine. Several *Xf*-cell-surface-binding peptides were selected from a random peptide library. For some of these peptides, the *Xf* cell target of binding and the stoichiometry of binding have been tentative identified. Evidence was obtained for a biologically relevant interaction between the selected peptides and *Xf* cells.

INTRODUCTION

It is likely that the development of grapevine cultivars resistant to *Xylella fastidiosa (Xf)* presents the best approach to long term, effective, economical and sustainable control of Pierce's disease (PD). Our strategy is to create transgenic rootstock(s) that will secrete a protein or proteins into the xylem for transport to scion xylem, where it will provide protection against insect vector-delivered *Xf*. An effective protein may kill *Xf* cells or merely interfere with the ability of *Xf* cells to colonize or spread in the scion xylem. Regardless of the mode of action, such proteins are here referred to here as anti-*Xf* proteins. No protein of the desired activity exists, and it is the immediate aim of this project to create anti-*Xf* protein(s). Several approaches have been taken. The approach that has been most productive is the selection of *Xf* cell-surface-binding peptides, as we describe in this report. Such peptides may be incorporated into a protein scaffold so as to generate a *Xf*-cell-surface binding protein. We have identified as a promising scaffold a protein of a T2-like bacteriophage: the tail fiber adhesion gp38 (Riede et al. 1987).

OBJECTIVES

1. Discover or develop peptides and proteins with high affinity for portions of MopB or other macromolecule that is displayed on the *Xf* cell exterior.
2. Test surface-binding proteins for their ability to coat *Xf* cells, for possible bactericidal activity or for interference with disease initiation following inoculation of grape or model plant with *Xf*.
3. In collaboration with the Gupta laboratory, develop gene constructions for chimeric proteins designed to bind tightly to and inactivate *Xf* cells; express and test the chimeric proteins for their effects on *Xf* cells in culture.
4. In collaboration with the Dandekar laboratory, prepare transgenic tobacco and grape expressing and xylem-targeting the candidate anti-*Xf* proteins; test the transgenic plants for resistance to infection by *Xf*

RESULTS

Objective 1 (Discover peptides and proteins with high affinity for macromolecules on the *Xf* cell).

Selecting peptides that bind to Xf cells

Xf cell-binding peptides were obtained by a combinatorial biology approach: selection from a random peptide library. The source of the random peptide library was a commercial kit (New England Biolabs "Ph.D.-12 Phage Display Peptide Library," designated here RP-M13) incorporating 12 amino acid residue random peptides at the amino end of the bacteriophage M13 adhesin protein pIII (Figure 1) (Anonymous 2004). The RP-M13 (~2.7 x 10^9 peptide sequences, with ~55 particles displaying any single peptide in a 10µL aliquot) was applied using "panning," a procedures involving multiple rounds (typically four or more) of selection in which the filamentous M13 particles bearing random peptides were exposed to the target (*Xf* cells). The target was washed, typically 8 times, and any remaining bound M13 was eluted and recovered, typically at pH 2.0-2.2. The eluted M13 was titered and amplified by inoculation of male *E. coli*. M13 progeny were partially purified before initiating the next round of selection (Smith and Scott 1993, Barbas et al. 2001).