CITRUS ADVANCED TECHNOLOGY PROGRAM

QUARTERLY & FINAL REPORTS: Control of Citrus Greening, Canker & Emerging Diseases of Citrus

SELECT PERIOD March 2014

(●) *Quarterly Report* ( ) *Final*

Proposal Title

Investigation of Tetracycline Analogs and Formulations Against HLB

Today's Date	Sponsoring Organization (drop-down)	Category (drop down)
11/11/14	Citrus Research and Development Foundation	Infection Consequences

REPORT UPDATE (500 words-It is not necessary in this public report to disclose your institution's proprietary information or intellectual property.)

Within the tetracycline family of compounds, a select subgroup of compounds have discreet and select activity against alpha-proteobacteria, including CLas, the agent responsible for Huanglongbing (HLB), while devoid of activity against human bacterial pathogens. Such selectivity against HLB by these compounds can be used to treat plants while sparing the possibility of antibacterial resistance, creating microbial agents or biocides in their own class of compounds affecting HLB alone.

Our efforts in tetracycline chemistry continue to produce the most highly active compounds found effective against the surrogate strain Liberibacter crescens, where most of the derivatives were 3 or more orders of magnitude more active than oxytetracycline.

Two of the most potent compounds derived from these screening studies, designated EBI-601 and EBI-602, are being studied in models of phloem transport in citrus and were found to be transported throughout the plant by either foliar or bark application of the formulated compounds.

This quarter, we have engaged in the synthesis and characterization of new derivatives of EBI-601 and EBI-602, modifying physico-chemical parameters related to size, electronic character and lipophilicity at chosen positions within the tetracycline nucleus, using chemical techniques of spanning substituent space. By creating an array of new compounds that are chemically tractable with commercial methods of synthesis, we will provide new compounds effective against HLB, and with the ability to product commercial quantities. While other methods of control are currently being studied under funding mechanisms supported here and by other agencies, these methods, including siRNA, older compounds already used and compounds from commercial libraries, may be of limited use due to high cost, low effectiveness, toxicity or therapeutic activity and use as human therapeutics.

Our compounds are currently effective against the surrogate Liberibacter strain, have no use in human medicine, have favorable biodistribution in the plant, are inexpensive, novel and patentable, and can be scale-up with starting materials in ready supply under contract agreement by prominent manufacturers.

The compounds synthesized this quarter have been fully characterized chemically and by MIC testing against the Liberibacter surrogate, represent some of the potentially most potent compounds found to date against HLB, the causative agent of citrus greening.

This study demonstrates for the first time that an effective and targeted microbicide can be chemically designed to combat agricultural diseases in commercially valuable crops.

PI First Name Mark

PI Last Name Nelson

Email mnelson@echelon-inc.com

Phone 774-571-8607

Organization Echelon Biosciences, Inc.

Project Number 775

Project Duration (years) 1 *Year of Project* 1

Total Funds (current year) $116,275.00

Form PR-12 Quarterly Reports **SUBMIT REPORT**

CITRUS RESEARCH AND DEVELOPMENT FOUNDATION, INC.