USDA-ARS/
U.S. Wheat and Barley Scab Initiative
FY14 Final Performance Report
July 15, 2015

Cover Page

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Fiscal Year:	FY14
USDA-ARS Agreement ID:	59-0206-4-008
USDA-ARS Agreement Title:	Application of Hormonal Biomarkers for DON-3-Glucoside Risk Assessment.
FY14 USDA-ARS Award Amount:	$ 58,489

USWBSI Individual Project(s)

USWBSI Research Category*	Project Title	ARS Award Amount
FST-R	Hormonal Biomarkers for Trichothecene Risk Assessment.	$ 58,489
	FY14 Total ARS Award Amount	**$ 58,489**

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Principal Investigator Date

* MGMT – FHB Management
FSTU – Food Safety, Toxicology, & Utilization of Mycotoxin-contaminated Grain
GDER – Gene Discovery & Engineering Resistance
PBG – Pathogen Biology & Genetics
EC-HQ – Executive Committee-Headquarters
BAR-CP – Barley Coordinated Project
DUR-CP – Durum Coordinated Project
HWW-CP – Hard Winter Wheat Coordinated Project
WES-CP – Western Coordinated Project
VDHR – Variety Development & Uniform Nurseries – Sub categories are below:
SPR – Spring Wheat Region
NWW – Northern Soft Winter Wheat Region
SWW – Southern Soft Red Winter Wheat Region

Project 1: *Hormonal Biomarkers for Trichothecene Risk Assessment.*

1. What major problem or issue is being resolved relevant to Fusarium head blight (scab) and how are you resolving it?

The toxic endpoints used to set regulatory standards for DON are growth retardation and emesis. The FDA has established a 1 ppm level of concern for DON in flour. These levels are in concurrence with Japanese, Canadian, and Russian standards. In contrast, the European Union has established regulatory limits for DON of 200 and 500-750 ppb for infant and adult foods, respectively. There are two important considerations concerning these standards. First, a 100 fold uncertainty factor had already been applied to the No Observed Adverse Effect Level (NOAEL) in mice to achieve the tolerable daily intake on which the 1 ppm estimates were derived. Second, the EU used an extremely conservative exposure estimate based on 95% maximum likelihood estimate of a probabilistic model. Currently, there is active discussion by CODEX on how to best harmonize regulations for DON and its congeners. Several research studies suggest these effects are mediated by neuroendocrine hormones. Thus any evaluation of DON-3-G toxicity should include measurement of these responses. Enteroendocrine cells (EECs) are one of the four primary intestinal cell subtypes that populate the epithelial layer of the GI tract. EEC normally sense the contents of the gut lumen and respond by secreting a range of peptide and amine hormones that can act on adjacent cells, afferent enteric neurons and more distal cells. These hormones control numerous digestive and physiologic functions. We propose to test the ***guiding hypothesis*** that *DON and DON-3-G differentially regulate hormone secretion EEC models from mice and mink.* Our research will be important because it will help discern whether DON-3-G is sufficiently toxic to include in the TDI for DON. The resulting data can be directly applied to DON safety assessments and enable determination of the accuracy of existing hazard data being used for establishing international guidelines.

2. List the most important accomplishments and their impact (i.e. how are they being used) to minimize the threat of Fusarium Head Blight or to reduce mycotoxins. Complete both sections; repeat sections for each major accomplishment:

Accomplishment: We have compared the anorectic effects of DON-3-G and DON in the mouse. While the thresholds and kinetics of the response were different, the effects of DON-3-G and DON were similar.

Impact: Using food refusal in mice as an endpoint, it might be appropriate to include DON-3-G with DON in safety assessment from chronic exposures

Accomplishment: We have compared the inflammatory effects of DON-3-G and DON in the mouse and found DON-3-G was largely incapable of inducing proinflammatory cytokine expression

Impact: In risk assessments of acute inflammatory effects of DON, it is not appropriate to include DON-3-G.

Accomplishment: We have compared the emetic effects of DON-3-G and DON in the mink and found DON-3-G was 40x less effective than DON causing vomiting.

Impact: In risk assessments of acute emetic effects of DON, it is not appropriate to include DON-3-G.

Training of Next Generation Scientists

Instructions: Please answer the following questions as it pertains to the FY14 award period. The term "support" below includes any level of benefit to the student, ranging from full stipend plus tuition to the situation where the student's stipend was paid from other funds, but who learned how to rate scab in a misted nursery paid for by the USWBSI, and anything in between.

1. **Did any graduate students in your research program supported by funding from your USWBSI grant earn their MS degree during the FY14 award period?**
   -Yes
   If yes, how many?
   -2

2. **Did any graduate students in your research program supported by funding from your USWBSI grant earn their Ph.D. degree during the FY14 award period?**
   -No
   If yes, how many?

3. **Have any post docs who worked for you during the FY14 award period and were supported by funding from your USWBSI grant taken faculty positions with universities?**
   -Yes
   If yes, how many?
   -2

4. **Have any post docs who worked for you during the FY14 award period and were supported by funding from your USWBSI grant gone on to take positions with private ag-related companies or federal agencies?**
   -no
   If yes, how many?

Include below a list of all germplasm or cultivars released with full or partial support of the USWBSI during the FY14 award period. List the release notice or publication. Briefly describe the level of FHB resistance. *If not applicable because your grant did NOT include any VDHR-related projects, enter N/A below.*

N/A

Include below a list of the publications, presentations, peer-reviewed articles, and non-peer reviewed articles written about your work that resulted from all of the projects included in the FY14 grant. Please reference each item using an accepted journal format. If you need more space, continue the list on the next page.

Zhou, H.R., Pestka, J.J., 2015. Deoxynivalenol (vomitoxin)-induced cholecystokinin and glucagon-like peptide-1 release in the STC-1 enteroendocrine cell model is mediated by calcium-sensing receptor and transient receptor potential ankyrin-1 channel. Toxicol Sci **145**, 407-417.

Wu, W., Zhou, H.R., Bursian, S.J., Link, J.E., Pestka, J.J., 2015. Emetic responses to T-2 toxin, HT-2 toxin and emetine correspond to plasma elevations of peptide YY and 5-hydroxytryptamine. Arch Toxicol. [Epub ahead of print]

Wu, F., Groopman, J.D., Pestka, J.J., 2014. Public health impacts of foodborne mycotoxins. Annu Rev Food Sci Technol **5**, 351-372.

Wu, W., Zhou, H.R., Bursian, S.J., Pan, X., Link, J.E., Berthiller, F., Adam, G., Krantis, A., Durst, T., Pestka, J.J., 2014. Comparison of anorectic and emetic potencies of deoxynivalenol (vomitoxin) to the plant metabolite deoxynivalenol-3-glucoside and synthetic deoxynivalenol derivatives EN139528 and EN139544. Toxicol Sci **142**, 167-181.

Wu, W., He, K., Zhou, H.R., Berthiller, F., Adam, G., Sugita-Konishi, Y., Watanabe, M., Krantis, A., Durst, T., Zhang, H., Pestka, J.J., 2014b. Effects of oral exposure to naturally-occurring and synthetic deoxynivalenol congeners on proinflammatory cytokine and chemokine mRNA expression in the mouse. Toxicol Appl Pharmacol **278**, 107-115.

Wu, W., Zhou, H.R., He, K., Pan, X., Sugita-Konishi, Y., Watanabe, M., Zhang, H., Pestka, J.J., 2014d. Role of cholecystokinin in anorexia induction following oral exposure to the 8-ketotrichothecenes deoxynivalenol, 15-acetyldeoxynivalenol, 3-acetyldeoxynivalenol, fusarenon X, and nivalenol. Toxicol Sci **138**, 278-289.

Pan, X., Whitten, D.A., Wilkerson, C.G., Pestka, J.J., 2014. Dynamic changes in ribosome-associated proteome and phosphoproteome during deoxynivalenol-induced translation inhibition and ribotoxic stress. Toxicol Sci **138**, 217-233.

Zhou, H.R., He, K., Landgraf, J., Pan, X., Pestka, J.J., 2014. Direct activation of ribosome-associated double-stranded RNA-dependent protein kinase (PKR) by deoxynivalenol, anisomycin and ricin: a new model for ribotoxic stress response induction. Toxins (Basel) **6**, 3406-3425.