USDA-ARS/
U.S. Wheat and Barley Scab Initiative
FY10 Final Performance Report
July 15, 2011

Cover Page

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Fiscal Year:	FY10
USDA-ARS Agreement ID:	59-0206-9-058
USDA-ARS Agreement Title:	Mechanisms and Biomarkers for Deoxynivalenol-induced Growth Retardation.
FY10 USDA-ARS Award Amount:	$ 87,805

USWBSI Individual Project(s)

USWBSI Research Category*	Project Title	ARS Award Amount
FSTU-R	Mechanisms and Biomarkers for Deoxynivalenol-Induced Growth Retardation.	$ 87,805
	Total ARS Award Amount	**$ 87,805**

James V Pestka 7/14/2011

Principal Investigator Date

* MGMT – FHB Management
FSTU – Food Safety, Toxicology, & Utilization of Mycotoxin-contaminated Grain
GDER – Gene Discovery & Engineering Resistance
PBG – Pathogen Biology & Genetics
BAR-CP – Barley Coordinated Project
DUR-CP – Durum Coordinated Project
HWW-CP – Hard Winter Wheat 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: *Mechanisms and Biomarkers for Deoxynivalenol-Induced Growth Retardation.*

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

This project addresses Goal #2 of the FSTU Action plan " Provide requisite information on DON/trichothecene safety issues to producers, millers, researchers, risk assessors and regulators." To achieve this goal , we tested the hypothesis that DON-induced growth retardation results from DON-induced cytokine-mediated SOCS-3 upregulation, which inhibits hepatic GH signaling, leading to reductions of growth factor(s) and weight gain. This hypothesis is being tested in the mouse model because the proposed and existing DON limits are based on studies in this species.

2. List the most important accomplishment and its impact (i.e. how is it being used) to minimize the threat of Fusarium head blight or to reduce mycotoxins. Complete both sections (repeat sections for each major accomplishment):

Accomplishment 1: We have confirmed that that oral DON-induced growth suppression correlates with the two clinically relevant growth-related proteins, IGFALS and IGF1.

Impact. We have confirmed the validity of one or more sensitive biomarkers of DON's growth effects that can also complement biomarkers of exposure in human studies. This research will update the science on which DON regulation is based, resulting in quantitative data that can be applied to DON-specific safety factors. It will ensure precision to DON regulation and balance consumer protection and food supply and is consistent with the goals of the Food Safety, Toxicology and Utilization of Mycotoxin-Contaminated Grain Research Area.

Accomplishment 2: We have determined in obese adult mice that modest DON exposure can reduce adipose weight and body weight without affecting lean weight.

Impact. These results suggest that DON exposure might have the unanticipated benefit of reducing obesity without causing wasting. This information will be an important consideration in risk assessment.

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 grant. Please reference each item using an accepted journal format. If you need more space, continue the list on the next page.

Publications

1. Amuzie, C. J., and Pestka, J. J. (2010). Suppression of insulin-like growth factor acid-labile subunit expression--a novel mechanism for deoxynivalenol-induced growth retardation. Toxicol Sci 113, 412-421.
2. Bae, H. Y., Gray, J. S., Li, M. X., Vines, L., Kim, J., and Pestka, J. J. (2010). Hematopoietic cell kinase associates with the 40S ribosomal subunit and mediates the ribotoxic stress response to deoxynivalenol in mononuclear phagocytes. Toxicological Sciences 115, 444-452.
3. Pestka, J. J. (2010). Deoxynivalenol: mechanisms of action, human exposure, and toxicological relevance. Archives of Toxicology 84, 663-679.
4. Pestka, J. J. (2010). Toxicological mechanisms and potential health effects of deoxynivalenol and nivalenol. World Mycotoxin Journal 3, 323-347.
5. Pestka, J.J. 2010. Deoxynivalenol-induced proinflammatory gene expression: Mechanisms and pathological sequelae. Toxins 2:1300-1317.
6. Flannery, B. M., Wu, W., and Pestka, J. J. (2011). Characterization of deoxynivalenol-induced anorexia using mouse bioassay. Food Chem Toxicol 49, 1863-1869.
7. Amuzie, C. J., Flannery, B. M., Ulrich, A. M., and Pestka, J. J. (2011). Effects of deoxynivalenol consumption on body weight and adiposity in the diet-induced obese mouse. J Toxicol Environ Health A 74, 658-667.
8. Kobayashi-Hattori, K., Amuzie, C. J., Flannery, B. M., and Pestka, J. J. (2011). Body composition and hormonal effects following exposure to mycotoxin deoxynivalenol in the high-fat diet-induced obese mouse. Mol Nutr Food Res 55, 1070-1078.

Presentations

1. Pestka, J. (2010) Trichothecene mycotoxins, macrophage activation and the ribotoxic stress response. Dept. of Microbiology and Molecular Genetics, Michigan State University
2. Flannery, B. (2010) Evaluation of insulin-like growth factor acid-labile subunit as a novel biomarker of effect for the mycotoxin Deoxynivalenol, Dept. of Food Science and Human Nutrition, Michigan State University.
3. Flannery, B., Amuzie, C., Ulrich, A, and Pestka, J.J. (2010) Deoxynivalenol ingestion prevents and ameliorates diet-induced obesity in the mouse. Toxicologist,. Annual Meeting of the Society of Toxicology, Salt Lake City, UT, March 2010.
4. Hattori, K., Flannery, B., Amuzie, C., and Pestka, J.J. (2010) Modulation of body fat mass and lean weight in deoxynivalenol-induced body weight reduction in the obese mouse. Annual Meeting of the Society of Toxicology, Salt Lake City, UT,.
5. Flannery, B. (2010) Mechanisms of deoxynivalenol-induced food and weight reduction in the diet-induced obese mouse. Microbiology and Molecular Genetics Scholarship Competition, Michigan State University.

6. Flannery, B., Amuzie, C., Ulrich, A, and Pestka, J. (2010) Ingestion of deoxynivalenol reduces diet – induced obesity in the mouse. Experimental Biology Meeting in Ventura, California.
7. Flannery, B. (2010) Characterization and mechanisms of deoxynivalenol-induced feed refusal in the mouse. Toxicology Night at Michigan State University.
8. Flannery, B., Pestka, J. (2011) Novel feeding bioassay for characterization of deoxynivalenol-induced feed refusal in the mouse. Annual Meeting of Society of Toxicology, Washington DC,.
9. Flannery, B. (2011) Mechanisms of deoxynivalenol-induced anorexia and growth suppression Gordon Conference on Mycotoxins and Phycotoxins. Waterville, ME.
10. Pestka, J. (2011). Vomitoxin, friend or foe?: Molecular mechanisms of a common mycotoxin. Food Research Institute, University of Wisconsin-Madison
11. Pestka, J. (2011). Ribotoxic Stress: Mechanisms and Models for Human Disease, Annual Meeting of Society of Toxicology, Washington DC.
12. Pestka, J. (2011). Role of ribotoxic stress and innate immune activation in trichothecene-induced iga nephropathy. Annual Meeting of Society of Toxicology, Washington DC.
13. Pestka, J. (2011) Vomitoxin, friend or foe?: Molecular mechanisms of a common mycotoxin. Alleghany-Erie Society of Toxicology,Pittsburgh, PA

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