USDA-ARS/
U.S. Wheat and Barley Scab Initiative
FY07 Final Performance Report (May 07 – May 09)
No Cost Extension for FY08
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Cover Page

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Fiscal Year:	2007
USDA-ARS Agreement ID:	59-0790-6-060
USDA-ARS Agreement Title:	Biomarkers of Low Dose Immunotoxicity of Deoxynivalenol in Mice.
FY07 ARS Award Amount:	$ 41,980

USWBSI Individual Project(s)

USWBSI Research Area*	Project Title	ARS Adjusted Award Amount
FSTU	Biomarkers of Low Dose Exposure to Deoxynivalenol in Mice.	$41,980
	Total Award Amount	**$ 41,980**

J Hendrich 7/9/09

Principal Investigator Date

* CBCC – Chemical, Biological & Cultural Control
EEDF – Etiology, Epidemiology & Disease Forecasting
FSTU – Food Safety, Toxicology, & Utilization of Mycotoxin-contaminated Grain
GET – Genetic Engineering & Transformation
HGR – Host Genetics Resources
HGG – Host Genetics & Genomics
IIR – Integrated/Interdisciplinary Research
PGG – Pathogen Genetics & Genomics
VDUN – Variety Development & Uniform Nurseries

Project 1: *Transformation and Field Testing of Transgenic Barley Lines.*

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

   There is little information available regarding the toxicity of deoxynivalenol (DON), the fungal toxin associated with wheat/barley scab and most commonly found in those grains, especially in doses close to the current voluntary "action" levels of 0.5 ppm (EU) or 1.0 ppm (US) in finished foods for human intake. Biomarkers for exposure to DON and more evidence regarding NOAELs and LOAELs (no and lowest observed adverse effect levels) for DON is urgently needed.

   We addressed this need with mouse model feeding studies within the range of 0-2 ppm DON, observing multiple cell surface markers of leukocytes in peripheral blood in young and old adult mice over 14 and 28 days of DON exposure as a means of assessing toxic effects of DON related to immune function. The rationale for this study design is that this time frame is recognized as a standard for immunotoxicity testing. Additionally, aging is known to suppress some aspects of human immune function, so an immunotoxic fungal toxin such as DON might be likely to cause further suppression, and is an important aspect of investigation to protect vulnerable populations.

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 all three sections (repeat sections for each major accomplishment):**

   Accomplishment: To find biomarkers of the grain fungal toxin, deoxynivalenol (DON), 8 w and 16 mo old male and female BALB/c mice were fed 0, 1 or 2 ppm DON for 14 and 28 d. We hypothesized immunotoxicity in BALB/c mice was greater with aging combined with deoxynivalenol (DON) exposure. By flow cytometry, in young female mice, the percentage of T helper cells in peripheral blood was inhibited at 2.0 ppm after 14 d, not after 28 d; integrin expression (VLA-4 and LFA-1) in neutrophils was inhibited at 2.0 ppm after 28 d; percentage of splenic macrophages were inhibited at 2.0 ppm after 14 d and 28 d. In young male mice, CCR7 expression that directs cells to the lymph nodes was inhibited in blood T helper cells at 2.0 ppm DON after 14 d and 28 d. In old female mice, percentage of $CXCR5^{+}$ B cells in the blood was inhibited at 1.0 and 2.0 ppm DON after 14 d, but that effect disappeared after 28 d (CXCR5 directs cells to the spleen, the main site of action of mature B cells); the percentage of T cytotoxic cells (CD8+) in blood was inhibited at 2.0 ppm DON after 28 d. Compared with the other three groups, old male mice had the greatest change in leukocyte surface markers: in blood, increased integrins in neutrophils were observed at 1.0 and 2.0 ppm DON after 14 d; and increased CCR9+ T cytotoxic cells targeting small intestine and decreased numbers of T cytotoxic cells were observed at 2.0 ppm DON after 28 d. These results suggest small intestinal inflammatory damage in old male mice exposed to DON. CCR10+ T helper cells and T cytotoxic cells were increased in male mice fed 1.0 ppm DON after 14 d, which suggested low dose of DON had some immune functional benefit transiently. Multiple surface markers changed only at 14 d, and not 28 d of DON exposure, suggesting that BALB/c mice adapted to DON exposure, or that this model which generally showed immunosuppression after 28 d masked DON toxicity at the later time point.

Impact: These findings support a NOAEL for dietary DON of less than 1.0 ppm, and support the need for additional studies in mice housed in groups rather than in social isolation which may have additional relevance to humans. That this study at least partly supported the hypothesis that old mice experience greater effects of DON has the impact that further studies of old mice and DON exposure are warranted.

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.

Wu, X., Kohut, M., Cunnick J., Bailey, T., Hendrich S. (2009) Effects of deoxynivalenol on circulating and splenic leukocyte and hematological response in BALB/c mice: dose response and time course. Food Addit. Contam. A 26: 1070-80.

Wu X. 2008. Deoxynivalenol alters circulating and splenic leukocyte and cell migration markers in interaction with time course and sex in young and old BALB /c mice. PhD Dissertation, Iowa State University Library, Ames, IA

Presentations

Wu X, Cunnick J, Kohut M, Hendrich S (2009) Immunotoxicity of deoxynivalenol in BALB/c mice: effects on circulating and splenic leukocyte and cell migration markers with time course and dose response. Abs. no. 767, The Toxicologist CD — An official Journal of the Society of Toxicology, Volume 103, Number S-1, March 2009.

Hendrich S, Wu X, Cunnick JE, Kohut M. (2008). Age and Sex differences in apparent adaptation to immunotoxicity of deoxynivalenol in BALB/c mice. Midwest AOAC meeting, Bozeman, MT, June 10, 2008.

Wu X, Kohut M, Cunnick J, Hendrich S (2008) Sex differences in apparent adaptation to immunotoxicity of deoxynivalenol. Abs. no. 2239, The Toxicologist CD — An official Journal of the Society of Toxicology, Volume 102, Number S-1, March 2008

If your FY07 USDA-ARS Grant contained a VDHR-related project, include below a list all germplasm or cultivars released with full or partial support of the USWBSI. List the release notice or publication. Briefly describe the level of FHB resistance. If this is not applicable (i.e. no VDHR-related project) to your FY07 grant, please insert 'Not Applicable' below.

Not Applicable