**USDA-ARS/**
**U.S. Wheat and Barley Scab Initiative**
**FY06 Final Performance Report (approx. May 06 – April 07)**
**July 16, 2007**

# Cover Page

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| **Fiscal Year:** | 2006 |
| **USDA-ARS Agreement ID:** | 59-0790-6-060 |
| **USDA-ARS Agreement Title:** | Biomarkers of Low Dose Immunotoxicity of Deoxynivalenol in Mice. |
| **FY06 ARS Award Amount:** | $ 43,029 |

**USWBSI Individual Project(s)**

| USWBSI Research Area* | Project Title | ARS Award Amount |
|---|---|---|
| FSTU-R | Biomarkers of Low Dose Immunotoxicity of Deoxynivalenol in Mice. | $ 43,029 |
| | **Total Award Amount** | **$ 43,029** |

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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
PGG – Pathogen Genetics & Genomics
VDUN – Variety Development & Uniform Nurseries

**Project 1:** *Biomarkers of Low Dose Immunotoxicity of Deoxynivalenol in Mice.*

**1. What major problem or issue is being resolved and how are you resolving it?**

We are trying to find out which markers of immunotoxicity and DON exposure provide the most consistent and sensitive indicators when doses of deoxynivalenol (DON) are fed that are within the range of 0-2 parts per million, or in other words, doses that may be found in the human food supply. Establishing these biomarkers of DON toxicity will help to establish a no-observed adverse effect level (NOAEL) for this important, widespread fungal toxin found in grains. We have approached this with a mouse model in which we fed young adult male and female mice 0, 0.25, 0.5, 1 or 2 ppm DON for 14 or 28 days (n = 10 per sex, timepoint and DON dose (200 total mice). We developed methods to quantify the main subpopulations of immune system cells in mouse blood (total mononuclear cells, B cells, T helper cells, T cytotoxic cells, granulocytes, monocytes, and compared the responses of these cells across DON doses. We are also attempting to detect DON in mouse plasma to determine the correlation between DON concentration and leukocyte responses. We have an HPLC method and have confirmed a limit of detection of ~ 10 ng DON/mL using HPLC/MS; analysis of mouse plasma samples is ongoing.

**2. List the most important accomplishment and its impact (how is it being used?). Complete all three sections (repeat sections for each major accomplishment):**

**Accomplishment:**

We identified the following statistically significant effects of dietary DON on mouse peripheral blood lymphocytes at the following timepoints:

Day 14:

Males showed suppressed T-cytotoxic cells at DON doses of 0.25-2 ppm, and suppressed B cells at 2 ppm DON.

Females showed suppressed total blood mononuclear (leukocytes) cells when fed 1 and 2 ppm DON; males showed no such suppression.

This suppression in females was due to suppression of T-helper and T-cytotoxic cells at 2 ppm, and suppression of B-cells at 1 ppm but not at 2 ppm DON.

Day 28:

Males showed no immunotoxic effects of DON.

Females showed suppression of monocytes at 0.5, 1 and 2 ppm DON.

**Impact:**

The most significant impact of these findings is that most of DON's immunotoxic effects were transient, suggesting that there might be ways to attenuate or prevent DON toxicity if the mechanism of this apparent adaptation to DON can be determined, and if that mechanism proved amenable to modulation. Adaptations in DON metabolism due to DON exposure seem to be worth further investigation.

Another significant impact of these findings is that a no-effect level for DON may be less than 0.25 ppm for 14 day exposures in males, and less than 1 ppm for 14 day exposures in females, but more than 2 ppm for males after 28 day exposures and less than 0.5 ppm for 28 day exposures in females. Investigation of the health significance of short term and seemingly transient suppression of T-cytotoxic cells, T-helper cells and total mononuclear

cells, and longer term suppression of monocytes by DON are research needs based on these findings.

Finding major differences between the sexes in response to DON indicates a need to examine the role of sex hormones in modulating the toxicity of this compound, and suggests that interactions between DON and other environmental chemicals (e.g., some pesticides) that may disrupt sex hormone function might be important to consider in assessing the effects of DON on human immune function.

**As a result of that accomplishment, what does your particular clientele, the scientific community, and agriculture as a whole have now that they didn't have before?**

The scientific community may have a better appreciation for the need to control DON contamination because low level exposures to DON did cause some immune cell alterations in this mouse model. The possibility of modulating or preventing DON toxicity is also suggested by this work, which may stimulate additional useful research activity.

**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, Hendrich S. Biomarkers of low dose DON immunotoxicity in Balb/C mice. Fd. Chem. Toxicol., in preparation.