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

## PROJECT 1 ABSTRACT

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Our **long-term aim** is to develop methods to **lessen the toxicity of foodborne fungal toxins in humans.** This aim requires development of animal models that are increasingly relevant to humans, in exposure dose and potential biomarkers (biological/chemical indicators of toxic responses). Our choice of toxicity to the immune system as an endpoint is highly relevant to human health in that such effects may be fatal in populations with less than adequate immune function (e.g., those suffering from malnutrition, HIV infection, elders and infants in general). Human immune impairment may also have serious economic consequences. The **hypothesis** of the current project are that **suppression of peripheral blood lymphocyte counts are a sensitive biomarker distinguishing a lowest observed adverse effect level from a no observed adverse effect level (a level of exposure that one may be reasonably certain will not cause harm) for dietary deoxynivalenol (DON) exposure**. Deoxynivalenol is the fungal toxin that occurs in general most commonly in grains, especially in wheat and its derived foods.

We will test this hypothesis by feeding 0, 0.5, 1 or 2 ppm DON to groups of 20 BALB/c mice (a strain of mice commonly used for immune system testing) (10 male/10 female) for 14 and 28 days, assessing peripheral blood lymphocyte (PBL) total and subpopulation counts using flow cytometry. PBLs are a major component of the immune system circulating throughout the body. Gut-associated lymphocytes and splenocytes (spleen cells) will also be quantified to determine if the suppression of PBL numbers is due to their migration to the gut or the spleen. These studies will determine the utility of PBL counts as biomarkers of DON exposure that could be readily adapted to studies of human DON exposure and toxicity. We will also identify crucial times of exposure to optimize the observation of the lowest observed toxic dose and non-toxic dose for DON.

Our choice of DON doses for these studies is founded on our previous studies showing decreases in lymphocytes by DON doses of 1 and 2 ppm, and the occurrence of such exposures being likely in human populations, especially where DON content of the food supply is not well regulated, as is the case for most of the world's human population. (We recently observed 4 ppm DON in a bread mix available in a local grocery store.)

We are well-positioned to perform these studies, given our backgrounds in fungal toxin and immunological research and our solid data in support of this approach. These studies will lead to validation of a human-relevant model for defining a dose of DON that is reasonably likely not to be harmful to the human immune system, forming the basis for further detailed mechanistic studies of toxicity of DON at realistic human exposures.