
Dr. Pestka has written more about DON that anyone I have seen. DON is prevalent in food crops, especially grains. DON can induce a CIRS-like picture in vitro. **NB:** One must ask what difference there is in human host defenses comparing ingested DON versus aerosolized DON?


DON is far more active in creating illness in animals than in humans. Levels of 1-5 microgram/kg/body weight (1 PPM) are tolerated. This level is massive when considering identification of trichothecenes in urine.


Dr. Pestka continues to study this fascinating toxin, finding (as in ochratoxin) a glucuronide in urine (**NB:** one that will likely be detected by ELISA). He feels that DON could be related to growth retardation (data not cited)

4. Pestka J. Deoxynivalenol-induced proinflammatory gene expression: mechanisms and pathological sequelae. Toxins (Basel) 2010; 2: 1300-17. In animals, DON causes robust activation of innate immune mechanisms. Human health effects are far more obscure. (**NB:** Dr. Pestka needs to be involved with our dietary mycotoxin/genomic response trial in humans!).


A robust urinary assay for trichothecone showed DON frequently in samples and was associated with cereals. Removal of cereals from the diet reduced DON identification.

Multiple metabolites of DON and other trichothecenes were identified, as well as the DON glucoside in beer production. (NB: These compounds would likely all give positive ELISA assays in urine.)


DON-glucoside is a ubiquitous trichothecene found in all 176 types of beer assayed. Maximum levels observed reached 37 micrograms/dl (370 ppb). Stronger beers had more DON metabolites.

No true virulence factor for invasive A. fumigatus has been identified.


Low concentrations of trichothecenes superinduce TNF but higher concentrations may suppress such expression.


Double bond between C9-C10 and the 12, 13 epoxide ring are essential structural features of the biological effects of trichothecenes. NB: Substitutions such as those seen with beta-tubulin-1 associated mutations could increase toxicity.


Terrific paper for chemistry lovers. Very few bacteria are sensitive to trichothecenes but there are significant differences in plant susceptibility to these secondary metabolites. Some probiotics detoxify DON by opening the epoxide ring. (NB: those who teach us that mycotoxins are made to kill bacteria need to read this paper. Time to get rid of that assumption.) Trichothecenes are amphipathic which means they can enter a cell by direct translocation (NB: this is a variant for the functioning of ionophores). Significant numbers of non-trichothecenes have structures shown by X-Ray crystallography to be ones that look like trichothecenes (NB: in ELISA assays).

Production of mycotoxins in vitro does not reflect what fungi do in humans. No Aspergillus isolated from human aspergillomas made aflatoxin or ochratoxin A.


Proteinases from Stachy contribute to lung injury.


Exposure to toxins induced inflammatory responses in lung tissue of mice. Transcriptional activation can occur as an antecedent to the inflammatory responses.


Incredibly convincing studies of inflammation induced by exposure to components of WDB continue to be produced by Dr. Rand and his various collaborators. Transcriptional responses are confirmed to occur following exposure to low molecular weight compounds found in WDB.


Induction of inflammation-gene responses is key for understanding curdlan toxicity. Dectin-1 and dectin-2 effects are related to gene activation.


Anti-fungals must be able to penetrate biofilms (NB: Most azoles really are ineffective attacking biofilms)


In vitro conditions permitted study of surgical specimens of fungal sinusitis. Biofilm formation was noted.

Fungal biofilm in sinuses only forms if there is pre-existing bacterial biofilm (not including H. influenza). Injury to epithelial defenses by a fungal cilia toxin (not identified) enabled proliferation of fungi. Fungal biofilm did not increase mucosal inflammation. (NB: this study is small and was done in sheep.)


In vitro biofilm growth created resistance to antifungal drugs. NB: Again a small in vitro study ignores the dynamics of mucus.


In culture and in vitro growth of A. fumigatus can upregulated genes for gliotoxin production.


Aspergillus fumigatus biofilms are described. Penetration of the complex mesh of fungal biofilms is needed to eradicate these organisms in vitro.


Early, but voluminous work. The role of infection with Aspergilli and Mucor are ones in which host defects in immune response must occur. A variety of forms of these organisms are presented with unique antigens for each for which a different host response must occur.


More from Dr. Waldorf. Anti-hyphal defenses are primarily neutrophil-driven, as in ochratoxin-formers. NB: Role of T reg cells unknown back then.


Conidia exposed to neutrophils reprogram their gene activity. No genes involved with toxin production were upregulated. Iron/copper assimilation is upregulated.

Reactive oxygen species arrest growth of Aspergilli. Neutrophil sequestration of iron is an important host defense (see paper 25 above).


Mucin is a highly glycosylated macromolecules (NB: > 50% carbohydrate, therefore low a(w)) that provide significant defenses against pathogens and environmental toxins. Comprehensive study.


Another very long paper. Cellular and molecular properties of mucin are complex and diverse.


Mucus provides important innate immune function by detoxifying noxious molecules. Reduction of intact mucin can predispose to airway disease such as cystic fibrosis


Airway goblet cells are the major sources of mucins. Release of inflammatory cell secretions and IL-4, IL-13 contribute to hypersecretion of mucus.


New interventions directed at mucin overproduction will have a role in prevention of illness.


Focus is on inflammatory mediators involved with mucus activity. T reg cell factors such as FOXA2 have key role.


Similar work as above paper 32.

Intriguing paper showing that IL-33 actually does all the bad things we don’t want for respiratory health. **NB:** TGF beta-1 can induce IL-33.


The same investigators as in paper 34. Add IL-12 and IL-18 to the list of adverse inflammatory mediators in airway hypersecretion and spasm.


Classic paper looking at goblet cells and illness. **NB:** The interaction of goblet cells and ciliated cells suggests a role for TGF beta-1 transforming cell types in upper airway respiratory epithelium.


Multiple studies disagree markedly on production of gliotoxin in immunocompromised patients infected with A. fumigatus. No conclusion re gliotoxin formation in tissues can be made. Additional information of geographic variability is needed. Agents that induce activation of the gliotoxin production cluster are not defined.

Key take home messages here are that DON is a ubiquitous trichothecone that can be detected in urine following consumption of foods and fermented beverages. Role of mucins in protection of mucus membranes is tied to innate and cell mediated immunity. Given low a(w) of mucins and goblet cell secretions it is unlikely that endogenous mycotoxin production is a factor in lung, nasal mucosa or sinus.