Biomonitoring data as a tool for assessing Aflatoxin B1 exposure of workers (BIODAF)

CARLO BRERA

Italian National Institute of Health (ISS)

December 14th, Rome
Among xenobiotics, mycotoxins, secondary metabolites of fungal origin, are one of the most harmful naturally-occurring hazards with high toxic potency and impact on human and animal health.

Peculiar characteristics of toxicokinetics and toxicodynamics associated to the intake of the parent mycotoxins and the formation *in vivo* of the corresponding metabolites makes the exercise to establish the role of mycotoxins in the occurrence of some pathologies quite hard.

Human BioMonitoring is generally considered to be an estimate of exposure, rather than a measure of health, and should be employed alongside environmental and food monitoring.
Project BIODAF

The aim is to produce data on the quali/quantitative assessment of metabolites deriving from aflatoxin B1 intake in workers operating in risky workplaces due to the presence of contaminated environmental dusts.
Main objectives

The specific objectives of BIODAF are the following:

1. To determine the estimated exposure of aflatoxin B1 by characterising the metabolic profile of some mycotoxins in serum and urine of workers potentially exposed

2. To validate specific biomarkers of exposure of aflatoxin B1

3. To characterise the risk derived from aflatoxin B1 (Evaluation of Margin of Exposure (MoE))

4. To collect evidences of exposure for orienting appropriate management activities by competent Authorities and stakeholders on mycotoxin risks, with the aim to mitigate the exposure of workers

5. To disseminate the produced data by its publication on international peer-reviewed journals
Common Features

Occupational settings with:

- High diversity of fungi
- High exposure to environmental dust

- Settings that are important economical sectors (food industries and farm companies)

- All located in Emilia-Romagna and Lisbon
The Project
Occupational Settings

- Cork Industry (n=19)
- Artisanal Bakeries (n=24)
- Industrial Bakeries (n=21)
- Swine Farm (n=25)
- Feed Company (loading/unloading area) (N=29)
to scrutinize the serum and urine samples for multimycotoxins presence focusing on AFB1 and AFB1 adducts (albumin-Lysine and N7-Guanine) with HRMS

- Method of Choice
- Method Validation
- Extraction Procedure (clean up, dilute and shot)
- Detection Technique
- LOD (g/L) LOQ (g/L)
- Reference materials
- Standards (adducts, $^{13}$C)
The Project Outline

- 29 exposed workers
- 30 non-exposed controls
- Morning urine drawn on two consecutive days (Monday and Friday)
- Collection of Food Questionnaires

AFM1 in urine:

<table>
<thead>
<tr>
<th>Groups and days</th>
<th>N (%) of Positive Samples</th>
<th>Mean ng/mL</th>
<th>(95%CI)</th>
<th>Range (ng/mL)</th>
<th>Median (ng/mL)</th>
<th>Interquartile Range (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed Workers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monday</td>
<td>23/29 (79.3)</td>
<td>0.031</td>
<td>(0.015–0.046)</td>
<td>(0–0.161)</td>
<td>0.009</td>
<td>0.052</td>
</tr>
<tr>
<td>Friday</td>
<td>18/29 (62.1)</td>
<td>0.040</td>
<td>(0.008–0.071)</td>
<td>(0–0.399)</td>
<td>0.006</td>
<td>0.030</td>
</tr>
<tr>
<td>Total</td>
<td>41/58 (70.7)</td>
<td>0.035</td>
<td>(0.018–0.052)</td>
<td>(0–0.399)</td>
<td>0.008</td>
<td>0.051</td>
</tr>
<tr>
<td>Non-Exposed Controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monday</td>
<td>23/30 (76.7)</td>
<td>0.024</td>
<td>(0.008–0.039)</td>
<td>(0–0.180)</td>
<td>0.008</td>
<td>0.013</td>
</tr>
<tr>
<td>Friday</td>
<td>23/30 (76.7)</td>
<td>0.030</td>
<td>(0.010–0.049)</td>
<td>(0–0.259)</td>
<td>0.014</td>
<td>0.032</td>
</tr>
<tr>
<td>Total</td>
<td>46/60 (76.7)</td>
<td>0.027</td>
<td>(0.015–0.039)</td>
<td>(0–0.259)</td>
<td>0.009</td>
<td>0.025</td>
</tr>
</tbody>
</table>
Workers invited to participated (signed informed consent)

Spot urine samples (most of them collected during lunch break)

Multibiomarker approach (AFB1, AFB2, AFG1, AFM1, ALT, AME, AOH, BEA, CIT, DH-CIT, DON, DON-3-GlcA, EnA, EnA1, EnB, EnB1, FB1, HT-2, HT-24-GlcA, 10-OH-OTA, OTA, Otα, 2´R-OTA, T-2, ZAN, ZEN, ZEN-14-GlcA, α-ZEL, β-ZEL, α-ZEL-14-GlcA, β-ZEL-14-GlcA, TEA, allo-TEA, Gliotoxin, STER)

Food consumption data – Food Questionnaires related to dietary habits in most of the groups, were collected.

Control group (n=19) – the same approach followed for the workers group.

Others samples collected – raw materials and settled dust.
Final Results

✓ January/February 2018

✓ Data will provide information on the mixture of mycotoxins with major relevance in each occupational setting

✓ Individuation of those variables, present in each setting, possibly influencing workers’ exposure.

✓ Identification of the most suitable and adequate risk management measures to undertake (this information will also be presented to the companies that collaborate in the study).
Thanks for your attention
carlo.brera@iss.it