Mass spectrometry imaging of small xenobiotics on *Danio rerio*: influence of molecular profiles modification as potential localization asset

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**Overview**

**Objectives**
- Develop a methodology to indirectly locate small xenobiotics hindered by ion suppression effect.
- Obtain information on the ions affected by the contamination.

**Methods**

- **Biological model**: *Danio rerio* WYTA
- **Xenobiotic**: Diazinon
- **Contamination**: 24 hours at 5µM
- **Sectioning**: cryosectioning after gelatin embedding
- **Mass spectrometry**: MALDI-FT-ICR
- **Data analysis**: Receiver Operating Characteristics

**Results**

- Brain and liver were highlighted as potential localization of diazinon which correlates with literature.
- Some affected ions were identified.

**Introduction**

Biolocalization is an information of choice when studies want to better understand a xenobiotic's effect on an organism. When dealing with lipophilic xenobiotics present in small quantities, this information is often hindered, especially if ion suppression effect is taken into account. However, even a small quantity of a contaminant is enough to have a significant effect on the molecular profiles of different tissues.

In this study we show that a statistical analysis with Receiver Operating Characteristic (ROC) can compare data sets of contaminated and healthy tissues from *Danio rerio* in order to highlight discriminant signals. Regions of interest where the contaminant could be found are thus identified.

**Methods**

**Samples**
- **Model**: *Danio rerio* wild type AB
- **Control sample**: 3
- **Cont. sample**: 3

**Contamination**
- **Contaminant**: Diazinon
- **Concentration**: 5µM
- **Time**: 24 hours

**Results**

- Optical image of a control fish (top) and a contaminated fish (bottom).
- Distribution of 739.479 ± 6mDa m/z

**Matrix deposition**
- **Instrument**: SunCollect II (SunChrom)
- **Matrix**: HCCA
- **Flux**: 5 – 5 – 10 µL/min
- **Quantity**: ≤50 nmoles/mm²

**Mass spectrometry imaging**
- **Instrument**: Solaris 8.6.4 (Bruker)
- **Source**: MALDI
- **Analyzer**: FT-ICR
- **Mass range**: 100 to 1500 Da
- **Raster width**: 40µm
- **Resolution**: 100,000 at 400m/z

**Data analysis**
- **Software**: SCiLS Lab 2016b (SCiLS)
- **Denoising**: Root Mean Square
- **Statistical tools**: ROC & Co-localization

**Tissue**

<table>
<thead>
<tr>
<th>Tissue</th>
<th># of discriminant ions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>11</td>
</tr>
<tr>
<td>Heart</td>
<td>1</td>
</tr>
<tr>
<td>Intestine</td>
<td>2</td>
</tr>
<tr>
<td>Kidney</td>
<td>0</td>
</tr>
<tr>
<td>Liver</td>
<td>12</td>
</tr>
</tbody>
</table>

**Conclusions**

- This method highlighted the brain and the liver as potential localization for the diazinon, which is in correlation to the literature.
- Some ions marked as discriminant were also be identified, which could be interesting for the understanding of the action mechanism of the xenobiotic.

**Perspectives**

- Confirm the presence of diazinon in the determined regions by laser microdissection coupled with LC or GC-MS/MS.
- Coupling of mass spectrometry imaging with ion mobility in order to distinguish the isobaric ions.