## P-054
## THE GENOTOXIC AND CYTOTOXIC EFFECTS OF OCHRATOXIN A AND T-2 TOXIN IN RATS BONE MARROW AND BLOOD CELLS

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Mycotoxins are deleterious secondary metabolites of microfungi that contaminate food worldwide. Determining the potential genotoxic and cytotoxic effects of mycotoxins is of great importance for the estimation and prevention of their damaging effects in humans, animals, and crops. Ochratoxin A (OTA) and T-2 toxin (T-2) belonging to the most abundant and harmful mycotoxins, can induce inhibition of DNA and RNA synthesis and oxidative stress in different tissues. Here we studied genotoxic and cytotoxic effects of OTA and T-2 in rat bone marrow and blood leukocytes. Rats were orally administered OTA or T-2 (25 μg/kg b.w./day) for 21 consecutive days. Bone marrow was flushed out with RPMI 1640 medium from rat femurs using a syringe, venous blood was collected in heparinized tubes. All samples have been studied in triplicates and used for analysis within 15-30 min after collection. Genotoxic effects were studied using single cell gel electrophoresis (comet) assay, % DNA in comet tail was used as the main parameter of genotoxicity according to OECD guideline. Cell viability was measured using trypan blue exclusion test.
OTA and T-2 demonstrated cytotoxic activity both in bone marrow and in blood leukocytes. OTA increased % DNA in the tail in bone marrow and blood leukocytes, while genotoxicity of T-2 was detected only in bone marrow cells. Previously it was shown that OTA may persist in the blood, since OTA binds very strongly to human serum albumin, from where actively can be transported into the cells, while T-2 is actively excreted from the organism. The manifestation of the effect of T-2 in bone marrow can be caused by its belonging to radiomimetic compounds; it is known that bone marrow is the main target tissue of this group of substances.
Thus our data suggest that both mycotoxins are genotoxic and cytotoxic for rats but exhibit the tissue-dependent effect.

## P-055
## NEUROTOXICITY AND EPIGENETIC EFFECTS OF OCHRATOXIN A *IN VITRO*

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Occurrence of mycotoxins in food and environment has been evidenced worldwide and is considered as a significant economical and health problem. Recently, it was reported that mycotoxins cause neuropsychological impairment or mental and emotional disorders but the mechanism of neurotoxicity of certain mycotoxins remains unknown. The correct model for risk assessment of mycotoxins' neurotoxicity is not clearly identified, that hinder the comprehensive characterization of mycotoxins' hazard to humans. In this work, we aimed to study the cyto- and genotoxicity, oxidative stress, and epigenetic changes, as well as reversible/irreversible neurotoxic effects of ochratoxin A (OTA) in human and mouse neuronal cells.
The human SH-SY5Y and mouse HT22 cell lines were selected as test-models. The cytotoxicity of OTA was assessed using calcein-AM/propidium iodide double staining; the genotoxicity of OTA was tested using CBMN assay. The DHE and FPG-comet assays were used to study the OTA induced oxidative stress. The epigenetic effect of OTA was investigated using methylation sensitive comet assay.
It was shown, that OTA is not cytotoxic at the concentration range of 2.5-30 μM in both cell lines. The genotoxic activity was revealed only in HT22 cells at the highest tested concentrations (15 and 30 μM). At the concentrations of 2.5-10 μM OTA induces epigenetic changes in HT22 cells, reflected by the increased level (up to 45%) of unmethylated CpG islands in DNA. The increased level of reactive oxygen species and oxidized purines were detected. All observed processes were reversible after single-dose treatment, but can be retained in a case of chronic exposure. OTA-induced epigenetic changes were not revealed in SH-SY5Y cells, but the low level and reversible oxidative stress was observed after OTA treatment. So, human and animal neuronal cells have different sensitivity against mycotoxin-induced toxicity and careful data extrapolation should be performed when use only animal data.

## P-056
## NEW KUNITZ-TYPE HCRG PEPTIDES OF SEA ANEMONE *HETERACTIS CRIS*

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Marine coelenterates, sea anemones, are a rich source of biologically active peptides. Apart from peptide toxins modulating Kv, Nav, ASICs channels and α-pore-forming toxins, they produce inhibitors of serine proteinases of Kunitz-type, BPTI-Kunitz family. Recently discovered pharmacological potential of representatives of Kunitz-type peptides produced by the species *Heteractis crispa* (Tabakmakher et al., 2015; Gladkikh et al., 2015; Sintsova et al., 2015; 2017) is conditioned by the phenomenon, typical for poisonous organisms, namely, by existence of the multigene families encoding Kunitz-type peptides. This leads to their molecular diversity and functional diversification aimed at expanding of the biological targets range of sea anemones preys and predators. These processes are caused by ancestral genes duplication and paralogs sub- and/or neofunctionalization resulted in Kunitz peptides acquisition of polyfunctionality, subtype-selectivity, and an appearance of analgesic, anti-inflammatory, and anti-histamine activities. Earlier multigene
HCGS family coding more than three dozen of *H. crispa* Kunitz-type HCGS peptides was revealed (Isaeva et al., 2012).
In this work HCRG peptides (33 amino acid sequences of which were derived from cDNA ones) forming distinct HCRG subfamily within HCGS family were found. These highly similar peptides and three native ones (Gladkikh et al., 2012; 2015) form a combinatorial library characterized by point mutations of amino acid residues (observed at both main and weak contact sites as well as along the entire length of the amino acid sequences) which are responsible for: (i) Kunitz homologous' capability to canonical or alternative interaction with a wide spectrum of serine proteinases; (ii) modulation of some subtypes of Kv channels and/or TRP receptors functional activity. Kunitz peptide residues functionally significant for interaction with the biological targets were predicted by molecular dynamic simulations.
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## P-057
## OREGANO ORDINARY (*ORIGANI VULGARIS*) AS A SOURCE OF β-CARYOPHYLLENE

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Origanum vulgaris belonging to the Lamiaceae family, which is widely