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Early proteomic changes induced by fusariotoxin single and combined exposures on human hepatocytes

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While the reality of mycotoxin co-contamination of food commodities is now well-established, the assessment of the toxicological impact of mycotoxin mixtures is still rare. Moreover, studies concerning the mechanistic cellular response to mycotoxins (alone or in mixture) are lacking. Among the infinite number of possible mycotoxin mixtures found, combinations of toxins from *Fusarium* spp. (called fusariotoxins) are particularly widespread in the North temperate zone of the world and therefore of interest. In this context, our main objective was to compare the cellular mechanisms involved in response to single and combined exposures of the human hepatocyte cell line HepaRG to two relevant fusariotoxins, deoxynivalenol and zearalenone. After 1 h of exposure with deoxynivalenol and/or zearalenone at low cytotoxic doses (IC10), proteomes of HepaRG cells were analyzed by LC-MS/MS and compared to the control condition without mycotoxin. Among the 3000 identified proteins per sample, 55 showed a significant enhanced or reduced abundance compared to the non-exposed cells. Interestingly, none of these 55 proteins were in common between the cells exposed to deoxynivalenol and those exposed to zearalenone. Noteworthy, very few proteins were common between the mixture and the toxins alone. Cells exposed to deoxynivalenol showed an increased expression of proteins involved in DNA topological changes, chromosome segregation and proteolysis, whereas zearalenone mainly induced changes for proteins involved in response to steroid hormone stimulus. Concerning the mixture, the main affected biological processes were, among others, cell cycle phase, DNA packaging and cell division. Thus, these results highlighted different cellular pathways responded to different single and combined mycotoxins exposures.

Biography

Marie-Caroline Smith completed her Engineering Degree in Biochemistry and she is currently pursuing PhD at University of Brest, France. She is working on "The impact of fusariotoxins co-exposure on human cells". More specifically, she is studying the cellular mechanisms of the human monocytic cell line THP-1 as well as the human hepatic cell line HepaRG, involved in the response to the exposure of one or more *Fusarium* mycotoxins in acute and chronic exposure conditions through toxicology and proteomic approaches. She recently published a review article entitled 'Natural co-occurrence of mycotoxins in foods and feeds and their *in vitro* combined toxicological effects'.

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