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Mass spectrometry application to molecular toxicology and biomarker discovery: carcinogen-modified histones

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Human exposure to chemical agents of drug, dietary, occupational or environmental exposure is a main public health concern, as a major cause of cancer. Despite, most of the chemically-induced cancers could be averted upon preventive measures, encompassing accurate monitoring and regulatory action, only a little over 100 compounds are currently classified as “carcinogenic to humans” by the International “Agency for Research on Cancer”. This is mainly a reflection of the difficulty in accurately assessing human exposure and classifying the carcinogenic potential of chemical agents. Therefore, more accurate and earlier compound-specific biomarkers of chemical carcinogenesis are urgently needed. Using the food contaminant and rodent carcinogen furan as model, the first evidence for *in vivo* occurrence of carcinogen-modified histones were recently provided by mass spectrometry-based methodologies. A furan-derived adduct was identified in liver histone 2B of rats treated with tumorigenic doses of furan. Taking into consideration that the formation of furan-derived DNA adducts is yet to be provided, furan-modified histone 2B may provide a toxicologically relevant furan-specific biomarker of carcinogenicity. Importantly, this adduct was identified prior to epigenetic modifications, which is consistent with the occurrence of carcinogen-modified histones at early stages of exposure. Recent advances on the detection of histone adducts with other chemical carcinogens suggest that these modifications are general in scope. Consequently, the covalent modification of histones by chemical carcinogens or their metabolites may provide relevant early compound-specific biomarkers of cancer. This is anticipated to be useful for accurate risk assessments, allowing efficient regulatory measures, and ultimately leading to decreased incidence of chemically-induced cancers.

Biography

Alexandra M.M. Antunes has completed his PhD at the age of 29 years from Universidade Nova de Lisboa (Portugal). She is Chemical Toxicologist, Principal Researcher of a team focusing on the use of covalent adducts formed with proteins (adductomics), directed towards the development of early biomarkers of chemical carcinogens and risk assessment of drugs used in chronic therapies, at Instituto Superior Técnico (Portugal). She has published more than 40 papers in reputed journals.

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