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Epigenetics: A Promising Tool to Decipher the Molecular Mechanisms of Pesticides Exposure and Health Effects

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Epigenetics is the study of heritable changes in gene expression that occur without a change in the DNA sequence or in other words, all meiotically and mitotically heritable changes in gene expression that are not coded in the DNA sequence itself. Several epigenetic mechanisms, including DNA methylation, histone modifications and microRNA expression, can be triggered by environmental factors. Pesticides are complex environmental contaminants which cause both acute and delayed health effects on human health. These effects may be simple to more severe leads to damage the nervous system, the reproductive system, whole body and may be cancer like diseases. Lamentably, despite of number of studies antecedently, there are no consensus among scientists or may say, the molecular mechanisms underlying such effects aren't fully understood. Several investigations have examined the effects of environmental exposures and epigenetic markers, and identified toxicants that modify epigenetic states.

Introduction

In the last century, a number of studies proved the detrimental effects of pesticides on human health. In recent times, a new approach aimed at evaluating different mechanisms by which pesticides could impact on human health, altering gene regulation has been developed. Among these new approaches, epigenetics seems a promising tool (Collotta *et al.*, 2013). Thus, understanding the molecular mechanisms able to mediate the effects of environment is of great importance. Epigenetics is the study of heritable changes in gene expression that occur without a change in the DNA sequence. Interestingly, epigenetic changes can be triggered by environmental factors. Environmental exposure to metals, persistent organic pollutants or endocrine disrupting chemicals has been shown to modulateepigenetic marks (Baccarelli and Bollati, 2009).

Several epigenetic mechanisms, including DNA methylation, histone modifications, and microRNA (miRNA) expression, can change genome function under exogenous influence, such

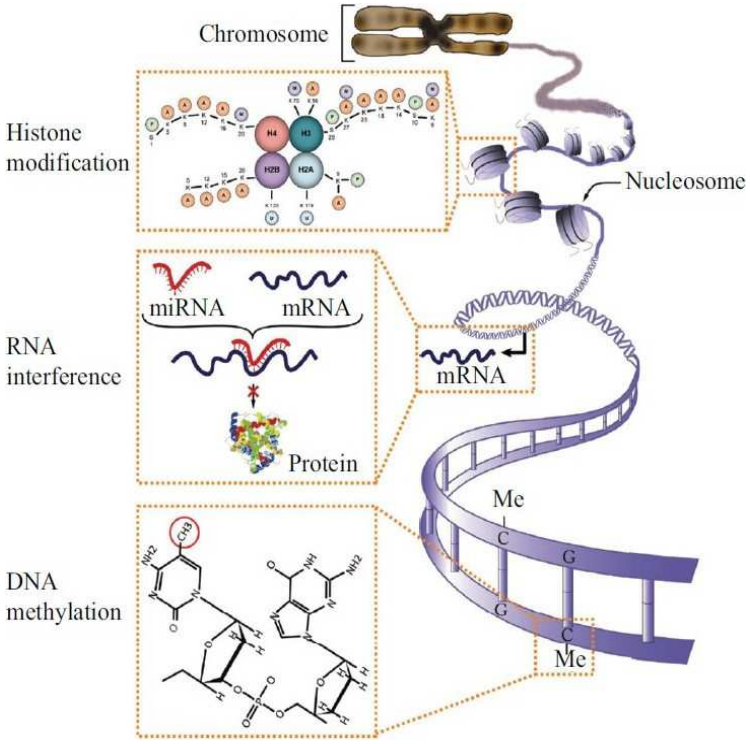
as environmental pollutants. Epigenetic changes may mediate specific mechanisms of toxicity and responses to certain chemicals. Furthermore such modifications might persist even in the absence of the factors that established them (Anway et al., 2006; Dolinoy, 2008).

Mechanisms of Epigenetics

Epigenetic modifications include DNA methylation, histone modifications, and microRNAs (Chuang and Jones, 2007).

1. **DNA methylation**

DNA methylation is a covalent modification, involved in regulating many cellular processes including chromatin structure and remodeling, X-chromosome inactivation, genomic imprinting, chromosome stability, and gene transcription (Grewal and Moazed, 2003; Reik et al., 2001). DNA methylation is heritable by somatic cells after cell division. Exposure to dichlorodiphenyltrichloroethane (DDT) alters the methylation pattern in the hypothalamus of young male rats. The DNA methylation system can be affected by exposure to high doses of organochlorine pesticides, methylmercury chloride or polychlorinated biphenyls. Pyrosequencing methylation analysis revealed that the high-dose groups generally decreased the methylation of CpG sites in the promoter of the tumor suppressor gene p16(INK4a) (Desaulniers *et al*., 2009).



2. **Histone modifications**

Histones modifications can regulate gene expression, chromatin remodeling, cell survival and cell death (Kouzarides, 2007). Exposure to environmental neurotoxic metals, pesticides and other chemicals is increasingly recognized as a key risk factor in the pathogenesis of chronic neurodegenerative disorders such as Parkinson's and Alzheimer's diseases (Kanthasamy *et al*., 2012; Kwok, 2010; Migliore and Coppede, 2009). Paraquat, a widely used herbicide, and the organochlorine insecticide Dieldrin, are among the environmental chemicals potentially linked with Parkinson's disease. Histone acetylation may represent the key epigenetic change in dopaminergic neuronal cells during neurotoxic insults.

3. **MicroRNAs (miRNA)**

MicroRNAs are single-stranded RNAs and plays role in gene expression regulation mediated by a control of messenger RNA (mRNA) stability or translation. The effects on the

epigenome caused by pesticides can be attributed also to a change in the miRNA expression profile, thus leading to changes in gene regulation which can explain the noxious effects that these chemicals have on human health. Cerri *et al*., 2011 evaluated the epigenetic effects of dichlorvos (DIC), an organophosphorus insecticide, in a porcine kidney epithelial cell line (PK15) in order to achieve a better understanding of its non-neuronal cytotoxicity.

Conclusion

Epigenetic modifications are relative stable over time and may be influenced by the environment. Exposure to pesticides may lead to epigenome modifications. Experimental, clinical, and epidemiological studies of epigenetic changes caused by pesticides exposure have increased our understanding of the mechanisms of action by which they can modify gene expression. Most of the studies conducted so far have been centered on DNA methylation, whereas only a few recent investigations have studied the effects on histone modifications and miRNAs.

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