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#### Regulation of gene expression by Xenobiotics and microRNA

Gene expression is regulated by various mechanisms at transcriptional and post-transcriptional levels. Transcriptional mechanisms involve activation of transcription factors upon ligand binding or activation of signal transduction pathways. Many foreign compounds can bind specific nuclear receptors (AhR, CAR, PXR, PPARs) leading to activation of expression of target genes. Toxicity of chemicals is dependent on specific signaling pathway that involves chemical activates. Such factors as structure of chemicals, gender and species of studied animals determine the degree and kind of toxic effects of the compound. We have investigated species-specific effect of phenobarbital and different chemical modification of 2,4,6-tryphenyldioxane-1,3 (TPD) on the cytochrome P450 (CYP) – key enzyme in xenobiotic metabolism. Selective effects of closely resembling compounds on CYP2B induction on transcriptional level have been uncovered with the help of Enzyme activity assays, Western-blot, gel shift analysis and RT-qPCR. Additionally, microRNAs play important role in post-transcriptional regulation of numerous genes, in particular of the cytochrome P450. The effects caused by xenobiotics can be attributed to changes in the miRNA expression profile, thus leading to changes in gene regulation. This can explain the detrimental effects that these chemicals have on human health. We used *in silico* methods and experimental approaches in order to investigate whether some xenobiotics like DDT and benzo(a)pyrene affect the expression of miRNAs through the activation of nuclear receptors (NRs): CAR (DDT) and AhR (BP), as well as estrogen receptor ER1 and ER2. The study showed that expression of microRNAs might vary under xenobiotic induction through NRs activation. This effect depends on the tissue type of experimental animals. The correlation between expression of microRNAs, host genes and target genes was shown. Thus, xenobiotics can dramatically change both protein coding genes and microRNA expression profile, greatly contributing to their toxic effects including carcinogenesis.

#### Biography

Lyudmila Gulyaeva, PhD, Doctor of Biology is currently a Professor of Molecular Biology and Biochemistry at Novosibirsk State University, Head of the Molecular Carcinogenesis Laboratory of Institute of Molecular Biology and Biophysics, Novosibirsk, Russia. She got her PhD in Biochemistry in 1986 and Doctor Degree in 2000. She has spent most of her scientific carrier studying drug-metabolizing enzymes and their associations with cancer. A special interest of her research is receptor-mediated mechanism of hormone-related cancer and role of microRNA in regulation of target genes. The results of her scientific activity were published in over 180 scientific papers.

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