Research 7:

Loss of RAR-α and RXR-α and enhanced caspase-3-dependent apoptosis in N-acetyl-p-aminophenol-induced liver injury in mice is tissue factor dependent.

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Background: Tissue factor (TF) activates the coagulation system and has an important role in the pathogenesis of various diseases. Our previous study stated that retinoid

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receptors (RAR-α and RXR-α) are released as a lipid droplet in monocrotaline/lipopolysaccharide (MCT/LPS)-induced idiosyncratic liver toxicity in mice. **Aim of work:** Herein, the interdependence between the release of retinoid receptors RAR-α and RXR-α and TF in N-Acetyl-p-Aminophenol (APAP)-induced mice liver toxicity, is investigated. **Methods:** Serum ALT level, platelet and WBCs counts, protein expression of fibrin, TF, cyclin D1 and cleaved caspase-3 in liver tissues are analyzed. In addition, histopathological evaluation and survival study are also performed. **Results:** The results indicate that using of TF-antisense (TF-AS) deoxyoligonucleotide (ODN) injection (6 mg/kg), to block TF protein synthesis, significantly restores the elevated level of ALT and WBCs and corrects thrombocytopenia in mice injected with APAP. TF-AS prevents the peri-central overexpression of liver TF, fibrin, cyclin D1 and cleaved caspase-3. The release of RXR-α and RAR-α droplets, in APAP treated sections, is inhibited upon treatment with TF-AS. **In conclusion**, the above findings designate that the released RXR-α and RAR-α in APAP- liver toxicity is TF dependent. Additionally, the enhancement of cyclin D1 to caspase-3-dependent apoptosis can be prevented by blocking of TF protein synthesis.
Key words: Tissue factor; N-Acetyl-p-Aminophenol; TF-antisense; RAR-α; RXR-α

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