Description for the general public

Numerous substances adversely affecting living organisms are constantly produced and released to the environment as a result of human industrial activity. This group includes polychlorinated dibenzo-*p*-dioxins, among which 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) is the most harmful dioxin. It was found that TCDD action results in a broad spectrum of pathologies including disturbances of immune, neural, and endocrine functions. In target cells, TCDD binds to the aryl hydrocarbon receptor (AhR). This results in a number of reactions, leading to synthesis of enzymes of cytochrome P450 family (CYP1) These enzymes are involved in dioxin metabolism and biodegradation. Interestingly, particular dioxin congeners differ in their toxicity level and susceptibility to biodegradation. It was shown that dioxin susceptibility to biodegradation depends on a chemical structure of its molecule. Results of previous research demonstrated that 2,7-dichlorodibenzo-*p*-dioxin (DiCDD), containing only two chlorine atoms within the molecule, displays low toxicity and is easily metabolized. TCDD, in turn, with four chlorine atoms in the molecule is highly toxic and resistant to biodegradation. Since it was shown that CYP1 enzymes are able to metabolize DiCDD, but not TCDD, in the current project we will attempt to explain molecular interactions underlying different toxicity of examined dioxins. To fulfill this aim, we will examine DiCDD and TCDD effect on gene expression, protein expression and catalytic activity of three CYP1 enzymes: CYP1A1, CYP1A2 and CYP1B1. Moreover, we will identify atomic interactions involved in the selectivity and affinity of DiCDD and TCDD binding to the active site of CYP1 enzymes. The results of the project will inspire future research concerning the mechanism of toxicity of TCDD and other xenobiotics, and may also allow to minimize negative effects of human industrial activity.