



Nucleic acid interactions and genome stability

Submitted by **RNDr. Ctirad Hofr, Ph. D.**

“Oponentský posudek habilitační práce”

The habilitation work of Ctirad Hofr is divided into three parts. The first part deals with the “description of changes in structure and thermodynamics of DNA induced by the binding of new and clinically used anticancer drugs derived from metal compounds“. In this chapter the interaction of cisplatin, transplatin, and other metal-based potential anti-cancer compounds with DNA (and to some limited extent also with DNA binding proteins) are investigated. The methods used are mainly differential scanning calorimetry, (temperature-dependent) UV absorption spectroscopy and circular dichroism determinations. Intellectually these studies started with a comparison of cisplatin with its (in terms of cancer therapy inactive) isomer transplatin and then was extended to further compounds, partially derived from cisplatin. This chapter is based on 8 original publications in international impacted journal (and one review in a Czech journal). This chapter has to be considered as the main chapter of this habilitation thesis for following reasons: 1) More than half (8 out of 15) of the all papers summarized in this thesis are devoted to this topic. 2) In 3 papers Ctirad Hofr is the first author, and thus his exposed contributions to these papers are documented. The mainly biophysical results described here are interesting and certainly internationally well recognized. The second chapter investigates the interaction of (full-length human, plant, and yeast) telomeric proteins with DNA. The methods used here are isothermal titration calorimetry, surface plasmon resonance, electrophoretic techniques, and fluorescence anisotropy based binding assays. This chapter is based on 4 original publications and an overview article in a Czech based journal. In one paper Ctirad Hofr is the first author and in a

recently submitted one the corresponding author. Again, internationally recognized results are presented and Ctirad Hofr's contributions to those papers are evidently significant. In the third chapter it is "demonstrated how functional binding studies and molecular structure data are combined to obtain a more comprehensive and detailed view of mechanism of double-stranded RNA recognition", summarized in 3 original papers. Although these papers appeared in very prestigious journals like Cell, Journal of Biological Chemistry or Genes and Development, I consider this chapter more as an addition than a crucial, decisive part of this habilitation thesis. Why? It is evident that for all 3 papers Dr. Hofr performed solely the steady-state fluorescence anisotropy experiments, which represent only a fragment in those comprehensive studies based on a large variety of molecular biological, biochemical, spectroscopic, and computational methods. Moreover, it is very likely that Richard Stefl and/or Frederic Allain, and not Dr. Hofr are here the intellectual fathers of those contributions.

Concluding, I would like to state that the habilitation thesis submitted by Dr. Hofr is fulfilling in terms of publications the criteria for a successful habilitation procedure at the "Masarykova Unverzita" in Brno. Consequently, I recommend accepting the submitted thesis as a part of the habilitation procedure at that university.

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