Evaluation of the PhD Thesis of – Alteration of the redox signaling in liver cancer cells by non-thermal plasma and laser irradiation – Barbora Smolková

In her work Ms. Smolková reveals the basic mechanisms of interaction between liver cancer cells with non-thermal plasma and laser irradiation. Current dissertation provides deep insight about very important, interesting, and timely question on modulation of redox signaling in cells via external physical cues. Redox reactions and redox signaling are among key regulators of various physiological and pathophysiological processes. Various physical factors (e.g., non-thermal plasmas, laser irradiation) are being more frequently utilized as modulators of redox balance in cells. However, molecular determinants of such interactions are not known.

Firstly, Ms. Smolková provides very nice literature overview on current state of the art in the field of cell interactions with non-thermal plasmas and laser irradiation. Further, the dissertation is divided into two main experimental parts. One part deals with cellular effect of non-thermal plasma. Second part discusses laser-cell interactions.

The main output of first experimental part is how air non-thermal plasma induces cell death in two hepatocellular carcinoma cell lines (HepG2 and Huh7). Ms. Smolková found that non-thermal plasma induces cell death via the formation of multiple intracellular reactive oxygen/nitrogen species. Her results showed a discrepancy in the superoxide accumulation and lysosomal activity in response to plasma in these cell lines, suggesting that plasma-triggered signaling cascades might be grossly different between HepG2 and Huh7.

Second experimental part of the dissertation deal with revealing molecular mechanisms of low-power laser-cell interactions. Ms. Smolková identified mitochondria as a sub-cellular “sensor” and “effector” of laser light non-specific interactions with cells. She demonstrated that despite blue (398 nm) and red (650 nm) laser irradiation results in similar apoptotic death, cellular signaling and kinetic of biochemical responses are distinct. Based on these data, it was concluded that blue laser irradiation inhibited cytochrome c oxidase activity in the electron transport chain of mitochondria. In contrast, red laser triggered excessive activation of cytochrome c oxidase. Moreover, Ms. Smolková showed that Bcl-2 protein inhibited laser-induced toxicity by stabilizing mitochondria membrane potential. Thus, cells that either overexpress or have elevated levels of Bcl-2 are protected from laser-induced cytotoxicity.

In conclusion, Ms. Smolková summarized that both non-thermal plasma and laser irradiation bias redox balance in cells via disturbance of accumulation and production

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of reactive oxygen species. This creates a foundation for finding generalized fundamental cellular effector of distinct physical cues.

Presented dissertation resulted into 4 publications published in impacted peer-reviewed journals, several conference contributions, and lectures. One of the publications is in very prestigious journal ***Cellular and Molecular Life Sciences***, which is ranked in ***TOP 10 %*** in the field of Biochemistry and Molecular Biology.

Overall, I evaluate the submitted dissertation as excellent; and I strongly recommend it for defense.

Sincerely,

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