



Human-Induced Radioresistance as a Possible Mechanism for Producing Biological Weapons: A Feasible Bridge between Radioresistance and Resistance to Antibiotics and Genotoxic Agents

Seyed Alireza MORTAZAVI¹, Farough KHADEMI¹, Mohammad MOTAMEDIFAR², Masoud HAGHANI³, *Seyed Mohammad Javad MORTAZAVI^{3,4}

1. Student Research Committee, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
2. Dept. of Bacteriology & Virology, School of Medicine, HIV/ AIDS Research Center (SHARC), Shiraz University of Medical Sciences, Shiraz, Iran
3. The Center for Research in Radiological Sciences, School of Allied Medical Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
4. Medical Physics and Medical Engineering Department, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

***Corresponding Author:** Email: mmortazavi@sums.ac.ir

(Received 11 Dec 2013; accepted 25 Dec 2013)

Dear Editor-in-Chief

Deliberate release of harmful biological agents such as bacteria and viruses which cause disease or death in humans, animals, or plants, an action that is usually referred to as a bioterrorism attack, is a global concern. Bacteria and viruses used in bioterrorism are typically found in our natural environment, but possibly the ability of these agents to cause illness, their resistance to current drugs, their ability for spreading into the environment (air, water and food) could be significantly increased by mutations. According to WHO, resistance of microorganisms to antimicrobial agents can lead to prolonged illness, greater risk of death and higher costs. Over the past years, investigators have generated extremely radioresistant bacterial species by directed evolution in *Escherichia coli*, a relatively radiosensitive bacterium (1). Radioresistance, a property which makes organisms capable of coping with intense levels of ionizing radiation can be found in certain extremophiles. *Deinococcus radiodurans*, one of the most radioresistant organisms known, is extremely resistant not only to ionizing radiation but also to UV, desiccation, and oxidizing and electrophilic agents. *Deinococcus*

radiodurans can withstand acute doses of ionizing radiation on the order of 10kGy (2). In other words, *Deinococci* are extremely resistant to the severe DNA damage caused by irradiation and oxidizing agents probably because their survival in nature is dependent on this resistance. It is found that the mechanism of DNA repair in *D. radiodurans* bacteria exposed to gamma radiation is a recA-dependent recombination process. It has been reported that *D. radiodurans* can mend over 100 double strand breaks (Successful repair without lethality, mutagenesis or rearrangement) following exposure to a dose of 10 kGy, while the majority of other organisms cannot mend only 2-3 double strand breaks per chromosome (3-6). We and other investigators have previously shown that pre-exposure to either small doses of ionizing radiation or non-ionizing radiation may induce resistance against subsequent exposure to high doses of ionizing radiation in plants, laboratory animals and human (7-11). Mechanisms such as alterations in the levels of cytoplasmic and nuclear proteins, increased gene expression, DNA repair and other processes may be involved in this type

of induced radioresistance. Using a Co-60 source, Harris et al. (1) repeatedly exposed *Escherichia coli* bacteria to a dose needed for 1% survival after 1 day. They had to increase the dose each time, as radioresistance increased. The findings of this study showed that the directed evolution, a method used in protein engineering to control the natural selection to evolve proteins or nucleic acids towards a user defined specific goal, can generate extremely radioresistant bacteria. Considering the analogy of the radioresistance pattern of *D. radiodurans*, this kind of human-induced radioresistance (directed evolution) possibly makes *Escherichia coli* bacteria resistant to all physical and chemical agents and may generate life threatening weapons. In this light, these experiments should be conducted carefully and all applicable ethical issues must be considered.

Acknowledgment

This study was supported by the Center for Research on Protection against Ionizing and Non-ionizing Radiation, Shiraz University of Medical Sciences (SUMS), Shiraz, Iran. The authors declare that there is no conflict of interests.

References

- Harris DR, Pollock SV, Wood EA, Goiffon RJ, Klingele AJ, Cabot EL, et al. (2009). Directed evolution of ionizing radiation resistance in *Escherichia coli*. *J Bacteriol*, 191(16):5240-5252.
- Norais C, Servant P, Bouthier-de-la-Tour C, Coureux PD, Ithurbide S, Vannier F, et al. (2013). The *Deinococcus radiodurans* DR1245 protein, a DdrB partner homologous to YbjN proteins and reminiscent of type III secretion system chaperones. *PLoS One*, 8(2):e56558.
- Minton KW, Daly MJ (1995). A model for repair of radiation-induced DNA double-strand breaks in the extreme radiophile *Deinococcus radiodurans*. *Bioessays*, 17(5):457-464.
- Minton KW (1994). DNA repair in the extremely radioresistant bacterium *Deinococcus radiodurans*. *Mol Microbiol*, 13(1):9-15.
- Daly MJ, Ling O, Minton KW (1994). Interplasmidic recombination following irradiation of the radioresistant bacterium *Deinococcus radiodurans*. *J Bacteriol*, 176(24):7506-7515.
- Daly MJ, Ouyang L, Fuchs P, Minton KW (1994). In vivo damage and recA-dependent repair of plasmid and chromosomal DNA in the radiation-resistant bacterium *Deinococcus radiodurans*. *J Bacteriol*, 176(12):3508-3517.
- Olivieri G, Bodycote J, Wolff S (1984). Adaptive response of human lymphocytes to low concentrations of radioactive thymidine. *Science*, 223(4636):594-597.
- Mortazavi SMJ, Shabestani-Monfared A, Ghiassi-Nejad M, Mozdarani H (2005). Radioadaptive responses induced in lymphocytes of the inhabitants in Ramsar, Iran. *International Congress Series* 1276(0):201-203.
- Mortazavi SMJ, Karam PA (2005). Apparent lack of radiation susceptibility among residents of the high background radiation area in Ramsar, Iran: can we relax our standards? *Radioactivity in the Environment*, ed Simopoulos ES (Elsevier), Volume 7, pp 1141-1147.
- Mortazavi SMJ, Cameron JR, Niroomand-rad A (2003). Adaptive response studies may help choose astronauts for long-term space travel. *Advances in Space Research* 31(6):1543-1551.
- Mortazavi SMJ, Mosleh-Shirazi MA, Tavassoli AR, Taheri M, Bagheri Z, Ghalandari R, Bonyadi S, Shafie M, Haghani M (2011). A comparative study on the increased radioresistance to lethal doses of gamma rays after exposure to microwave radiation and oral intake of flaxseed oil. *Iranian Journal of Radiation Research (IJRR)*, 9(1):9-14.