# POTENTIAL OF UV RADIATION PROTECTION BY THE EXPRESSION OF *drwH* GENE AND ANTIOXIDANT RELATED GENES OF *Deinococcus radiodurans* R1

**By**

**KHAIRUNISA AMIRA BINTI AHMAD**

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The prolonged exposure to sunlight is detrimental for the cells as they are exposed to high energy electromagnetic radiation from ultraviolet (UVA: 320 – 400 nm; UVB: 290 – 320 nm; UVC: 200 – 290 nm). UV radiation (UVR) can directly or indirectly affect vital biomolecules by producing reactive oxygen species (ROS). It is known that *Deinococcus radiodurans* R1 (*D. radiodurans* R1) can tolerate high amount of UVR. One of the reasons for the tolerance by *D. radiodurans* R1 apart from its powerful gene repair and the presence of carotenoid is due to the high expression of *drwH* gene that encodes for LEA protein upon exposure to UVR. The expression of *drwH* gene affecting the amount of ROS quantified using 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA) in *D. radiodurans* R1 because high expression of *drwH* gene is able to lowering down the level of ROS in the cells. High expression of *drwH* gene after UVC radiation also affecting the cell viability of *D. radiodurans* R1 as the percentage of bacterial cells killed after UVC radiation is lower as compared to UVA radiation. Total RNA is extracted from *D. radiodurans* R1 after irradiation to examine the expression fold changes of *drwH* gene and other antioxidant related genes that encode for antioxidant enzymes like superoxide dismutase, catalase and peroxidase by using RT-qPCR technique. LEA protein is believed to function as a chaperone or molecular shield to other proteins. Therefore, it is valuable to know whether *drwH* gene is able to affect the expression of antioxidant related genes. The expression fold of *drwH* gene is high after UVC radiation as compared to UVA radiation with the highest amount of 240.03 fold at 12 h of UVC radiation but lowest at 6 h with the value of 92.86 fold. The lower expression fold changes at 6 h of UVC radiation might be explain by higher expression fold changes of antioxidant related genes during that time. However, the expression of *drwH* gene does not explain the effect on antioxidant related genes, but the increased of both expressions lowered the level of ROS and preventing the decreased in cell viability. Then, *drwH* gene is cloned into *Escherichia coli* (*E. coli*) BL21 (DE3) but the difference in cell viability between wild type and

recombinant BL21 is little after UVA radiation but after UVC radiation, the cell viability of recombinant *E. coli* BL21 (DE3) is higher than wild type *E. coli* BL21 (DE3) after 12 h of irradiation. In conclusion, *drwH* gene is capable to provide protection against a high energy UVR and increased the viability of the cells as compared to low energy UVR. High expression fold of *drwH* gene and antioxidant related genes might lowering down the level of ROS production after UV radiation and this is contributing to the new insight on the dynamics of ROS and *drwH* gene relationship.

**Keywords:** Cell viability, *Deinococcus radiodurans* R1, *drwH* gene, LEA protein, radiation.

**SDG:** GOAL 3: Good Health and Well Being, GOAL 4: Quality Education, GOAL 13: Climate Action.

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**POTENSI PERLINDUNGAN SINARAN UV MELALUI EKSPRESI GEN *drwH* DAN GEN-GEN BERKAITAN ANTIOKSIDAN DARIPADA *Deinococcus radiodurans* R1**

Oleh

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Pendedahan berpanjangan kepada cahaya matahari memudaratkan sel kerana ia terdedah kepada sinaran elektromagnet bertenaga tinggi daripada ultraungu (UVA: 320 – 400 nm; UVB: 290 – 320 nm; UVC: 200 – 290 nm). Sinaran ultraungu (sinaran UV) boleh menjejaskan biomolekul penting secara langsung atau tidak langsung dengan menghasilkan spesis oksigen reaktif. Adalah diketahui bahawa *Deinococcus radiodurans* R1 (*D. radiodurans* R1) boleh menerima jumlah sinaran UV yang tinggi. Salah satu sebab toleransi oleh *D. radiodurans* R1 selain daripada pembaikan gennya yang berkuasa dan kehadiran karotenoid, adalah disebabkan oleh ekspresi gen *drwH* yang tinggi yang mengkodkan protin LEA apabila terdedah kepada sinaran UV. Ekspresi gen *drwH* mempengaruhi jumlah spesis oksigen reaktif yang dikira menggunakan 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA) dalam *D. radiodurans* R1 kerana ekspresi gen *drwH* yang tinggi mampu menurunkan tahap spesis oksigen reaktif dalam sel. Ekspresi gen *drwH* yang tinggi selepas sinaran UVC juga menjejaskan kadar kebolehhidupan sel *D. radiodurans* R1 kerana peratusan sel bakteria yang mati selepas sinaran UVC adalah lebih rendah berbanding sinaran UVA. Sejumlah RNA diekstrak daripada *D. radiodurans* R1 selepas penyinaran untuk memeriksa perubahan lipatan ekspresi gen *drwH* dan gen-gen berkaitan antioksidan yang mengekod kepada enzim-enzim antioksidan seperti superoksida dismutase, katalase dan peroksidase dengan menggunakan teknik tindak balas rantai polimerase kuantitatif masa nyata. Protin LEA dipercayai berfungsi sebagai pendamping atau perisai molekul kepada protin-protin lain. Oleh itu, adalah penting untuk mengetahui sama ada gen *drwH* mampu mempengaruhi ekspresi gen-gen berkaitan antioksidan. Lipatan ekspresi gen *drwH* adalah tinggi selepas sinaran UVC berbanding sinaran UVA dengan jumlah tertinggi 240.03 kali ganda pada 12 h sinaran UVC tetapi terendah pada 6 h dengan nilai 92.86 kali ganda. Perubahan ekspresi yang lebih rendah pada 6 h sinaran UVC mungkin dijelaskan oleh perubahan ekspresi yang lebih tinggi daripada gen-gen berkaitan

antioksidan pada masa itu. Walau bagaimanapun, ekspresi gen *drwH* tidak menerangkan kesan ke atas gen-gen yang berkaitan dengan antioksidan, tetapi peningkatan kedua-dua ekspresi menurunkan tahap spesis oksigen reaktif dan menghalang penurunan kebolehhidupan sel. Kemudian, gen *drwH* diklonkan ke dalam *Escherichia coli* (*E. coli*) BL21 (DE3) tetapi perbezaan kebolehhidupan sel antara *E. coli* BL21 (DE3) jenis liar dan rekombinan adalah sedikit selepas sinaran UVA tetapi selepas sinaran UVC, kadar kebolehhidupan sel *E. coli* BL21 (DE3) rekombinan adalah lebih tinggi berbanding jenis liar selepas 12 h penyinaran. Kesimpulannya, gen *drwH* mampu memberi perlindungan terhadap sinaran UV bertenaga tinggi dan meningkatkan kadar kebolehhidupan sel berbanding sinaran UV bertenaga rendah. Ekspresi tinggi gen *drwH* dan gen-gen berkaitan antioksidan mampu menurunkan kadar pengeluaran spesis oksigen reaktif selepas sinaran UV dan ini menyumbang kepada pendekatan baharu tentang dinamik hubungan spesis oksigen reaktif dan gen *drwH*.

**Kata Kunci:** *Deinococcus radiodurans* R1, gen *drwH*, kebolehhidupan sel, protin LEA, radiasi.

**SDG:** MATLAMAT 3: Kesihatan yang Baik dan Sejahtera, MATLAMAT 4: Pendidikan Berkualiti, MATLAMAT 13: Tindakan Memerangi Perubahan Iklim.

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**TABLE OF CONTENTS**

## LIST OF TABLES

## LIST OF FIGURES

## LIST OF APPENDICES

## LIST OF ABBREVIATIONS

| | |
|---|---|
| °C | Degree Celsius |
| % | Percent |
| µg | Microgram |
| µL | Microliter |
| Abs | Absorbance |
| $^1O_2$ | Singlet oxygen |
| bp | Base pair |
| CAT | Catalase |
| cDNA | Complementary deoxyribonucleic acid |
| DNA | Deoxyribonucleic acid |
| DCF | 2',7'-dichlorofluorescein |
| DCFH | 2',7'-dichlorodihydrofluorescein |
| DCFH-DA | 2',7'-dichlorodihydrofluorescein diacetate |
| $H^+$ | Hydrogen ion |
| $H_2O$ | Water |
| $H_2O_2$ | Hydrogen peroxide |
| h | Hour |
| IPTG | Isopropyl-ß-D-thiogalactoside |
| LB | Luria-Bertani |
| LEA | Late Embryogenesis Abundant |
| MAAs | Mycosporine-like amino acids |
| mL | Milliliter |
| mM | Millimolar |

| | |
|---|---|
| mW | Milliwatt |
| $O_2$ | Oxygen |
| $O_2^-$ | Superoxide radical |
| $OD_{600}$ | Optical density at 600 nm |
| OH• | Hydroxyl radical |
| PAR | Photosynthetically active radiation |
| POD | Peroxidase |
| PCR | Polymerase chain reaction |
| qPCR | Quantitative polymerase chain reaction |
| RNA | Ribonucleic acid |
| ROS | Reactive oxygen species |
| RT-qPCR | Real-time quantitative polymerase chain reaction |
| SOD | Superoxide dismutase |
| TGY | Tryptone, glucose and yeast |
| UV | Ultraviolet |
| UVR | Ultraviolet radiation |
| WHy | Water stress and hypersensitive response |
| WST-8 | 2-(2-methoxy-4-nitrophenyl)-3-(4-nitrophenyl)-3-(2,4-disulfophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium |

# CHAPTER 1

## INTRODUCTION

Sunlight is comprised of visible light and ultraviolet (UV) with the wavelength of 10 to 700 nm. Terrestrial and marine organisms consume sunlight to drive their own light-driven respiratory or photosynthetic reaction (Wang et al., 2014). The penetration of UV Radiation to the Earth's surface exposing the organisms to high energy radiation after extended time. The region of UVA (320 – 400 nm) and UVB (290 – 320 nm) only, is able to penetrate to the surface because the energy of UVC (200 – 290 nm) is used to drive the production of ozone layer at the atmosphere. However, these range of UV radiation also could cause detrimental effects on the vital biomolecules of the cell (Preira, 2015).

UV radiation will cause the production of high energy reactive oxygen species (ROS) like superoxide anion ($O_2^-$), hydroxyl radical (OH•), singlet oxygen ($^1O_2$) and hydrogen peroxide ($H_2O_2$), after the incidence of oxidative stress in the cells (de Jager et al., 2017). The production of ROS can also be detected *in vivo* of the cells by a few fluorescence probes that will form fluorescent product which then will be quantified by using spectrofluorometer (Sing et al., 2013).

The photoprotection function by a few compounds in the cells will help to reduce the lethal impact of the production of ROS by the exposure to UV radiation. The first line of defence contributed by the role of small secondary metabolites that has the ability to scavenge ROS-formed. Then, the production of ROS also can be reduced or change to a higher stability molecule by antioxidant enzymes like superoxide dismutase, catalase and peroxidase (Lei et al., 2016). Interestingly, for human, melanin pigment has been an important compound for the screening of UV radiation in which the darker skin person tends to be less susceptible to the detrimental effects of UV radiation (Jenkins & Grossman, 2013). Besides that, there is a presence of protein which has a role in the tolerance to multiple number of abiotic stresses. It is usually found in plant but also present in other organisms, called Late embryogenesis-abundant (LEA) proteins that is believed to protect the cells from abiotic stress such as cold, drought, or high salinity (Liu et al., 2019).

*Deinococcus radiodurans* R1 *(D. radiodurans* R1*)* is an extremophile which can be found in radioactive soils on nuclear waste sites and on deserts. This is due to its ability to survive upon exposure to ionizing radiation [≥12,000 Gy (gray; absorbed radiation dose)], ultraviolet (≥1,000 J/m$^2$), and desiccation (years) (Qi et al., 2020). It is a robust organism because it has systems with a capability for DNA repairing, DNA damage exporting, desiccation and starvation recovery, and genetic redundancy (Li et al., 2016). In this research project, *D. radiodurans* R1 which is radioresistant microorganism has been chosen to study the effects of exposure towards UV radiation and the generation of photoprotective compounds due to its mesmerizing systems in combating radiations. In addition,

the presence of LEA protein in *D. radiodurans* R1 showed that it provides protection against dehydration and oxidative stress and also showed a chaperone like manner or a molecular shield as it increases the expression and activity of antioxidant enzymes during stress condition (Jiang et al., 2017).

The exacerbating effect of UV radiation on biomolecules is the main problem that have been directing this research project. The UV radiation has been a concern on living matters because it has the ability to ionize matter by inducing the production of ROS and render a deleterious effect on the cells. The discovery of LEA protein in *D. radiodurans* R1 showed that it is competent to protect the cells against oxidative stress when the incorporation of ROS, $H_2O_2$ into the cells does not causing a harmful effect for them. In addition, UV radiation is one of the contributors for the induction of oxidative stress in the cells, but little information is known whether the exposure to UV radiation will increase the production of ROS in *D. radiodurans* R1 as it is an extremophile.

This gap of knowledge motivates for the study of LEA protein which perhaps activated and protects the cells against UV radiation. Besides, in this study, the universal role of LEA protein is also tested by assessing the survivability of *Escherichia coli* (*E. coli*) BL21 (DE3) which carry the *drwH* gene that encodes for LEA protein from *D. radiodurans* R1 upon exposure to UV radiation.

Therefore, the objective of this research project is to study the regulation of *drwH* gene that encodes for LEA protein in the protection against exposure to UV radiation. This main objective will be supported by the following objectives:

1. To assess the responses of *D. radiodurans* R1 upon exposure to UV radiation.
2. To determine the expression level of *drwH* gene and antioxidant related genes in *D. radiodurans* R1 upon exposure to UV radiation.
3. To examine the effect of *drwH* gene from *D. radiodurans* R1 on the cell viability of *E. coli* BL21 (DE3) upon exposure to UV radiation.

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