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EDUCATIONAL SECTION

Deinococcus radiodurans

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Deinococcus radiodurans (DeiRa) is a remarkable organism. Its properties of extreme resistance to environmental damage and ionising radiation command the attention of the cancer research community for the insights which it may bring to the understanding of cytotoxic and radiotherapy treatment resistance.

INTRODUCTION

Deinococcus radiodurans (DeiRa) is a poly-extremophile bacterium. It survives in a variety of environments of extreme radioactivity and ultraviolet radiation, genotoxic chemicals, heat, dessication and severe acceleration and deceleration forces which are lethal to almost all other cellular species.

DeiRa was first identified in 1956 as a surprising contaminant of heavily irradiated canned food. Its radioresistance allows it to survive 1.5 million rads of gamma irradiation, some 3000 times more than that tolerated by human cells.[1] Radiation disrupts chromosomal DNA structure and function by oxidative damage, causing large numbers of single and double strand breaks which usually prove fatal to other cells. The survivability of DeiRa relates to the specific organisation of its chromosomes, to the redundancy and multiplication of key segments of its DNA, and to the range of highly efficient and multiple molecular DNA repair mechanisms.[2]

MOLECULAR STRUCTURE

The genome of the bacterium is one of a large number which have recently been fully sequenced. This allows a complete analysis of the functional biology, and detailed comparisons with the genomes of a variety of other bacterial species and of more complex organisms, including the fruit fly, mouse and man. Unusually, DeiRa comprises two circular chromosomes, which are 2.65 and 0.41 million DNA base pairs long, and two smaller circular DNA molecules, or plasmids, of 177 000 and 45 000 base pairs.[3] The organisation of repeat sequences of DNA every 50 000 bases along the genome is likely to provide protective redundancy, with between 4 and 10 copies of the complete genome in each bacterium.

THE BIOLOGICAL RELEVANCE OF DEIRA

DeiRa testifies to the survivability of DNA based life forms in environmental conditions far more extreme than those tolerated by higher organisms. It may shed light on the evolution of life on Earth in the early planetary conditions, and provide for the transmission of viable life through space to other planets and moons. It also finds practical industrial applications. For example, the selective genetic engineering of strains with enzymes to metabolise a range of toxic organic compounds such as toluene within radioactive waste will render the consolidation and further management of such wastes much easier. The fixation of mercury by engineered DeiRa provides for new ways of cleaning and separating heavy metal wastes.[5] These industrial processes are known as bioremediation.

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ITS RELEVANCE TO CANCER RESEARCH

Cancer cells are characterised by a number of features which are displayed in extreme form by DeiRa. They express variable radioresistance, and degrees of redundancy of DNA in aneuploid cells. DNA repair is a normal housekeeping function in all cells, and many thousands of spontaneously arising DNA breaks are repaired in each cell each day. Ionising radiation hugely increases the frequency of DNA strand breaks.[3] DieRa exhibits a number of molecular defence mechanisms. It expresses a variety of proteins, which undertake recombinational DNA repair. These include

the nucleoside diphosphate hydrolase (Nudix),[W1] ligase and endonuclease families of proteins are ubiquitous in living organisms and particularly widely expressed in DeiRa. They have specific molecular actions and receptors which allow for the design of cytotoxic inhibitory drugs to destabilise the cancer cell;

the carotenoids which give DeiRa a distinctive red colour may act as free radical scavengers after DNA damage;

the cell wall provides further protection, with three or more layers of complex membrane lipids and a thick peptidoglycan layer conferring additional radioresistance;

the RecA proteins confer particularly efficient repair of the DNA double stranded breaks which usually prove fatal to cells.[4]

The system thus provides a variety of experimental models for the mechanisms of resistance to drugs and ionising radiation in normal and diseased mammalian cells.

CONCLUSIONS

It may be inappropriate to extend the comparisons too far between a prokaryotic bacterium and a multicellular eukaryotic tissue system. However, the experimental and molecular insights provided by DeiRa are likely to find practical applications in cancer therapy. The rapid expansion in molecular sequencing and comparative genomics is providing for new insights into cancer cell biology from across the spectrum of living organisms and from unlikely origins. Advances in therapeutics may well come from cross fertilisation of ideas and techniques from this spectrum, and it is helpful to broaden thinking 'outside the envelope' of eukaryotic cancer cells in the search for useful models and practical progress.

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FURTHER READING

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