Foreword


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One of the major historical milestones that will retrospectively mark out the twentieth century will probably be the harnessing of nuclear energy for peaceful purposes. The opportunities offered by the many uses of ionizing radiation and radioactivity in the study of living organisms and in medical applications far outweigh the fears they inspire. Indeed, the already widespread use of radiation-based techniques in everyday medical prevention, observation and treatment often goes unnoticed. The usefulness of X rays, scanners and anticancer radiotherapy is seldom challenged by those who benefit from them. In addition, increasing awareness of the role of human activity in the «greenhouse» effect and its consequences on the evolution of the biotope actually argues in favor of nuclear energy production, which generates less carbon dioxide than burning other fuels. Admittedly, there are still legitimate concerns about the disposal and fate of radioactive waste, the consequences of accidental exposure to radiation, the risk of which can never be nil, and the effects of chronic exposure to low or very low level radiation. A more thorough understanding of the interactions of ionizing radiation with living matter, which is the essential aim of radiobiology, is therefore needed to address these issues.

The work conducted in this area both in France and internationally over the last few years has given rise to a number of fundamentally important notions that will be briefly discussed in this issue of *Clefs CEA*.

First of all an ever-richer and complex intermeshing of concepts, from the initial damage by radiation to the expression of cell response, have been noted. These concepts include cytotoxicity and cell suicide, production of genetic mutations and chromosomal aberrations, induction of carcinogenic transformation and associated genomic instability, and the modulation of gene expression with the transduction in cascade of effector signals.

Fuller knowledge of the processes involved in the faithful enzymatic repair of DNA - and in misrepair, and a better understanding of their genetic control, have demonstrated the extent of their interaction with other essential functions of the cell economy: replication, transcription, dynamic organization of chromatin, genetic recombination and probably differentiation during embryo growth.

The result of this is that current research is focusing more and more narrowly on the analysis of molecular interactions between several objects. Modern methods and techniques of structural biology are expected to contribute to this field of multiple associations among proteins or between proteins and nucleic acids. Recent approaches applied to the biochemical analysis of complexes of extremophilic organisms (e.g., those adapted to high temperatures or very high levels of radiation) suggest that if these molecular objects were combined differently, but in an organized way, new rules of cellular function might appear. These might then make survival possible in unpredictable environmental conditions.

Finally, it has become evident that certain essential functions have conserved an extraordinary stability over evolutionary time, including those involved in the repair of radio-induced damage. For example it has been found that from bacteria right through to man the processes of recognition and repair of wrongly paired DNA bases are remarkably well conserved. This demonstrates the central role of these mechanisms, which are involved in both the preservation of the continuity of species (faithful repair) and the introduction of biodiversity (misrepair). The occurrence of some severe pathologies can be ascribed to faults in these processes, e.g., predisposition to certain cancers or early aging observed in some syndromes.

Various laboratories at the Atomic Energy Commission (CEA) and the National Scientific Research Center (CNRS), together with the National Agronomic Research Institute (INRA), have all at some time or another in the course of their research work over the last five years made a contribution to these different areas. The efforts of the National Institute for Health and Medical Research (INSERM) in the field of biological effects of radiation have concentrated specifically on epidemiology. Regular concertation between the life sciences divisions of these different bodies has made it possible to avoid duplication, develop synergy and forge links based on common methodologies initiated by one participant. The development of DNA biochips by CEA and the interest that various CNRS groups are showing in this domain are a shining example of joint effort. The contribution of European researchers - English, Dutch and German - in collaboration with various French laboratories has been remarkable. In certain precise areas (e.g., coupling of repair with other vital functions) these associations, facilitated for example by European Community contracts, are stealing a lead over American and Japanese research.

It is still difficult to publish radiobiological results in major non-specialized journals. Important papers have nevertheless been published in the last five years in Science, Nature, Cell, The Proceedings of the National Academy of Science, USA and EMBO Journal (of the European Molecular Biology Organization). Some of these report particularly important findings concerning the detection of certain radio-induced lesions using ultra-sensitive methods, the formation of repair complexes by base excision with their mechanism of action, and the nature of the repair of double-strand breaks and the molecular players involved.
Continued close coordination between institutions and efficient management of resources, especially of young well-trained staff (the role of postgraduate qualification in radiobiology is important here), together with unswerving support from the Ministry in charge of Research should ensure that the French contribution to this high-level research area keeps on growing.
The political context in France and elsewhere in the world still often suffers from deeply ingrained misunderstandings and unease about nuclear power, even though the economic arguments for its maintenance are barely challenged. Fuller control over the action of radiation on living organisms, and reasoned comparison with other hazards such as tobacco abuse, traffic accidents and a range of industrial pollution, are the best line of defense against misleading information.

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