*Acta Biotheoretica* **43**: 279–280, 1995.


# IDEAS IN THEORETICAL BIOLOGY

## WHY ANIMALS HAVE TUMOURS

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## ABSTRACT

From the viewpoint of an evolutionary biologist, carcinogenesis should be looked upon as a protective mechanism against destruction of DNA. Because genes expressed in embryonic cells are covered and protected by heterochromatinization, they are the most appropriate 'alternate genes' compared to genes that are expressed already in somatic cells. When DNA-damage occurs, the embryonic genes can be activated. Some somatic cells exhibit some features of embryonic cells.

## HYPOTHESIS

A large number of DNA-damaging physical or chemical factors that are mutagens in bacteria are carcinogens in animals. It is well known that most mutations are harmful or even lethal to the cell. To survive in an environment where mutagens are apt to spread, organisms have to do all that they can to reduce this harmful effect of the DNA-damage. During evolution living creatures have evolved some DNA-repair systems e.g. photoreactivation, SOS response. Keeping the genetic information constant in somatic cells of adult animals is particularly critical because every cell has an important role in a complicated machinery. Once one part would not acts properly, the whole body would be affected. In bacteria almost all the genes are single-copied, once they are damaged by mutagens, the only way to survive is to repair this damage. In contrast, animal cells have many copies of genes or gene families, some of them are expressed in embryonic cells and some others are expressed in somatic cells of the adult animals. Thus animal cells exposed to mutagens could not only repair their damaged genes but also express other genes with the same function and which have not been damaged. After the embryonic stage some parts of chromosomes are heterochromatinized, which is generally believed to inhibit the activity of the embryonic genes. Due to the tight package by heterochromotinization, these genes are covered so that they have relatively low chance to get damaged by mutagens. Thus embryonic genes are the most appropriate 'alternate genes'. When the somatic cells of adult animals are exposed to mutagens, these 'alternate genes' might be activated and then take the place of the mutagen-damaged genes. This does not mean that only when a gene has been damaged by mutagens this 'alternate gene' can be activated. There should be a

complex, multistep response to mutagens or their damage e.g. pyrimidine dimer, like the SOS regulatory system of Escherichia coli (Little et al., 1982). When the DNA is damaged, an inducing signal is produced, the inducing signal then activates some modulators or inactivates some repressors. After an amplified chain reaction some parts of the chromosomes are deheterochromatinized and the embryonic genes can be activated. Because all the embryonic genes are normally expressed at the same stage, they are activated or inhibited in a similar way. One or more embryonic genes can be activated by the interaction of a mutagen and DNA, at the same time. As all the embryonic genes are suited for rapid proliferation of embryonic cells, the effect of the mutagen would cause the DNA-damaged cells to proliferate rapidly, and thus form a tumour. The resemblances between tumour cells and embryonic cells such as high aerobic glycolysis, pattern of isozymes is created simultaneously. Those mutagens that could not lead to the production of the inducing signal are not carcinogeneous.

Would life take one disaster to avoid another? Of course not. Tumour growth exerts an increasingly disturbing action on the host through infiltration and pressure on normal tissues, obstruction of vital organs, competition for available nutrients and so forth. Most tumours do not do any harm to their host until their cells proliferate to a large number or metastasize. Without vascularization it is likely that most tumours never would grow beyond a diameter of 1-2mm and would remain localized to the primary site for several years or even decades because passive diffusion cannot effectively provide nutrients for all the cells nor can waste products adequately diffuse out of the spheroid into the surrounding medium or matrix (Blood et al., 1990). The phenotypes of avascular tumours, tell us that not all tumours are harmful. Here the early stage of carcinogenesis should be looked upon as a mechanism to substitute or to repair damaged DNA. Even though bacterial SOS response is a DNA repair system, it always introduces some mutations as a side effect, which can be harmful. However, in critical conditions the most important is to survive, it is still better than death with some precisely repaired DNA. Similarly for carcinogenesis. It is well worth taking the risk of producing malignant tumours for the somatic cells of adult animals exposed to DNA-damaging factors.

## REFERENCES

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