Ukrainian Society of Cell Biology

International conference

Advances IN CELL BIOLOGY BIOTECHNOLOGY

11-13 October 2015

PROBABILISTIC MODEL OF CARCINOGENESIS AND PROBLEMS IN ESTIMATING MODEL PARAMETERS

***Vladimir G. Knigavko*, Olga V. Zaytseva, Marina A. Bondarenko,**
Liliya V. Batyuk, Tatyana R. Kocharova
Kharkiv National Medical University, 4 Lenina ave., Kharkiv, 61022, Ukraine
Email address: vknig@mail.ru

It is assumed [1] that an individual's genotype has a certain number (up to eight according to different data) of genes, which in the event of damage (loss of function) of all such genes, the cell shall undergo malignant change. In the following, such genes will be called a-genes.

The mutations that damage a-genes occur in a random manner. Hence, an individual's genotype can have a different number of such genes, and with time, this number decreases.

Study [2] has suggested a probabilistic mathematical model of cell malignant change. From this model, it follows that the distribution function (F (t)) of the time of development of a cancer disease in an individual is described by the following expression:

$$F(t) = 1 - \left(1 - \left(1 - \beta^{\frac{t}{T}}\right)^{k}\right)^{N},$$

where $\beta = 1 - \alpha$; α is probability of a-gene damage during one cell cycle; t is time elapsed since embryo formation, T is duration of cell cycle, k is initial amount of a-genes in an individual's genotype, and N is number of cells of a given type in the body. Thereat the study uses a simplifying assumption that T does not change with age.

In particular, from this model it follows that, at $k < 3$, the average time of formation of a tumour is less than a year, and at k = 7, this average time exceeds 100 years.

To analyse the model, it is necessary to estimate the probability of presence in an individual's genotype of a certain number of a-genes for the entire human population. More precisely, it is necessary to estimate the distribution of the number of a-genes in the population. Knowing this distribution would allow, for instance, to estimate the rate of growth of oncological diseases as a function of improving treatment quality because such improvement of quality stipulates increasing survivability of individuals with a small initial value of parameter k, thereby increasing the probability that such an individual will be able to sire.

Such an estimate can be obtained using two methods. The first method assumes calculating the probability of variation in the number of a-genes in gametes, with subsequent re-evaluation to obtain the above distribution. This method involves solving nonlinear systems of equations.

The second method assumes using experimental (clinical) data on the dependence of oncological morbidity on an individual's age to solve the problem considered. The second approach is simpler; however, it requires a big volume of statistical data, which is not yet available.

1. Гродзинський Д.М., Радіобіологія. К.: Либідь, 2000. 448 с.
2. Книгавко В.Г., Радзишевская Е.Б., Бондаренко М.А. Математическое моделирование канцерогенеза // Біофізичний вісник.- 2010. Вип. 25 (2).- С. 93-100.