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REVIEW ARTICLE

CAN A SOIL AGROBACTERIAS' PLASMIDS INDUCE CANCER CELLS IN PLANTS, ANIMALS AND HUMAN?

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ABSTRACT

The results of our research provided during the many years with plant, animal and human cells based on the scientific evidences, it is possible to argue that the application of billions of tons chemicals asxenobiotics, espesially high doses of nitrogen pollutions in soil, water and environment as a new factor of the biosphere evolution can be considered one of the triggers of mutations and tumour cells in eukaryotic organisms - in plants, animals and humans.

INTRODUCTION

Taking this opportunity, I would like to outline some of ideas on the origin and mechanism of formation of tumour cells that is beginning of cancerdiseases,while linking with the origin and ever increasing dissemination of annual pollutions of environment, caused by xenobiotic, first of all, the nitrogen and its various compounds. It is known that there are only two ways of providing a plant with nitrogen nutrition de novo: 1) Biological – based on symbiotic nitrogen fixating Agrobacteria tumifaciens and other free-living microorganisms; 2) Chemical – basedon the application of the industrial nitrogen fertilizer to the soil. In general, the production of nitrogen fertilizers, a very high energetic and expensive process, costs six times more than phosphorus and sixteen times higher than potash producing. In 1913, German scientists F.Gaber and K.Bosh proposed ammonia method of binding atmospheric nitrogen. Now, using this principle, hundreds of factories all over the world produce millions of tons of air bound nitrogen annually. Three-quarters of its production goes to fertilizer. Notwithstanding these factors, expansion of production continues. Thus, in 2000, in the USA alone, production costs of nitrogen fertilizer was 50 bln US Dollars a year. The total biological nitrogen fixation on the planet is about $1{,}7x10^8$ tons per year, while the global industrial synthesis of nitrogen is more $4x10^7$ tons per year. By the early 1980s, the world had produced more than 62 million tons of nitrogen fertilizer in the form of active substance.

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The figure was 72 million by the early 1990s, and 92 million by 2000 and about 112million tons by 2014s. Moreover, more than half of the produced nitrogen fertilizer is not utilaised by the agricultural plants and is a very dangerous pollutant of the human environment, water resources, agricultural products, etc. At present, such a global environmental pollution with nitrogen is a major concern worldwide, since nitrogen compounds, entering the acidic gastric environment of animals and humans, quickly turn into a potentially mutagenic and carcinogenic form. Nitrogen of these compounds are absorbed into the blood, firmly fixed instead of oxygen. This causes a dangerous blood disease –methemoglobinemia in human body, particularly in children («Blue baby»), which is often fatal. Based on the scientific evidences, it is possible to argue that the chemical production and application of billions of tons of nitrogen to the soil and environmental pollution is a new xenobiotic factor in the evolution of the biosphere and can be considered one of the triggers of mutations and tumour cells in eukaryotic organisms - in plants, animals and humans. Cancer - one of the most widespread and incurable diseases of the previous century.

Currently, there are more than 300 theories about the origin of cancer: physiological, stress, carcinogenic, virus, phage, mutagenic ... etc. However, while not ignoring their implications for science and their right to exist, we must recognize that the problem of the origin and nature of cancer is still open. The situation can be expressed by the phrase of the Russian fable - "things are there", as cancer remains incurable and a disease of man. As a researcher working for more than

forty five years of plant physiology and soil microbiology, space and cell biology, environmental genetics and theory of mutations, I still, with the continuous attention and interest, follow the development of new concepts of the mechanisms of cancer. Among various approaches and theories, I am most attracted to two scientific theories of the origin of cancer, which is closest to my vision of the problem:

1. Genetic theory advanced by Academician N.P. Dubinin, a renowned scientist in the field ofgeneral genetics, mutation theory and space biology (1969);
2. Paul Davies and Charles Lineweaver, from Arizona State University and Australian National University, theoretical physicists working in the field of astrobiology, searching for life beyond the Earth,have proposed a theory of cancer based on its ancient evolutionary roots (2012).

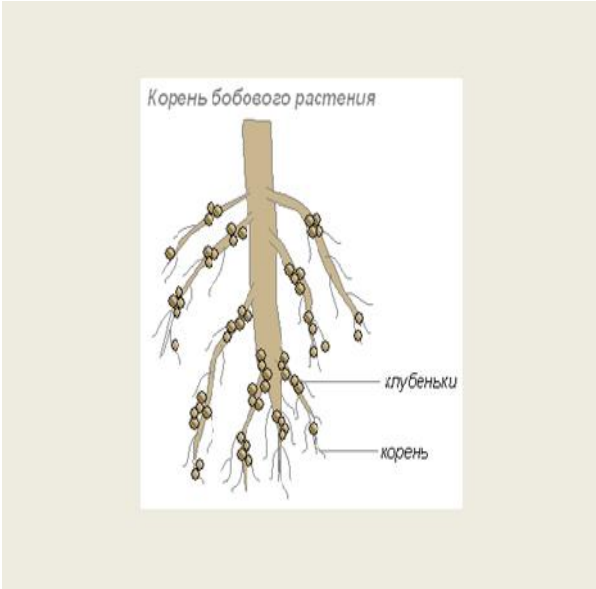


Fig. 1.The root of the legume with tubercles

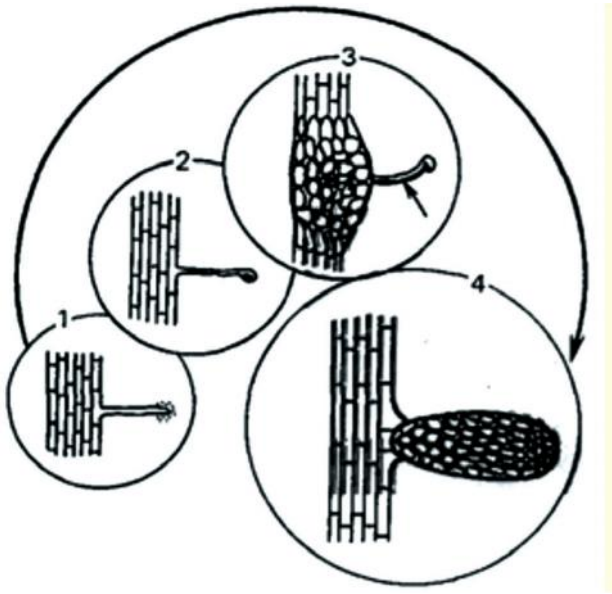


Fig.2. A scheme of formation of root nodules (1-attachment of bacteria, 2-winding of root hairs,3-formation infectious strand, 4- nature root tuber)

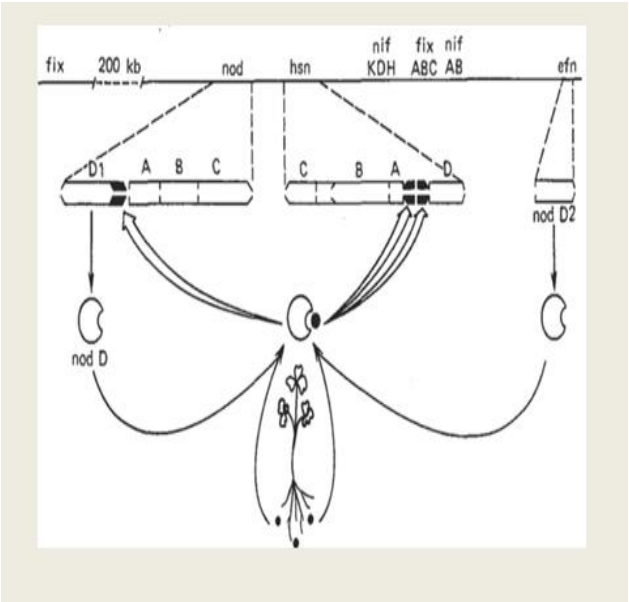


Fig.3. Organizational scheme of Nif- genes

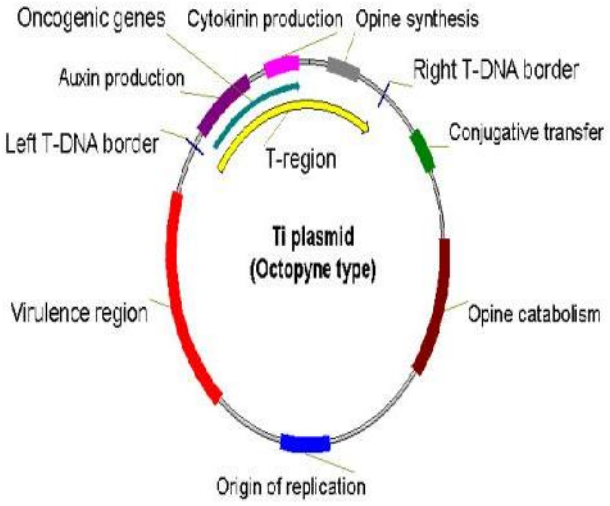


Fig. 4. Ti-plasmid A.tumefaciens with oncogenic genes

In my opinion, these concepts, while being closely interrelated, complement each other. Many years of research and reflection led me to the conclusion that the state of cancer cells in all eukaryotes (plants, animals and humans) are virtually identical and very similar to the state of bacterial cells. They infinitely multiply by division and there is no difference, in principle, that allows differentiation of these processes. Perhaps, it is in this sense the role of the emergence of the first Mother cell on the Earth and the importance of Ti-plasmids (Figure 4. The plasmid with Nif - operons and oncogenes) becomes apparent in the evolution of cellular life forms. Because of communality of nucleic acids, as the basic structure of the genetic material of all life forms on Earth, Ti – Plasmid (tumour inducing factor) can transfer from the initial free-living symbiotic or other microorganisms to eukaryotic genomes (plants, animals and human cells), and by regulation of auxin and cytokinin balances to induce initial callus or cancer cells.

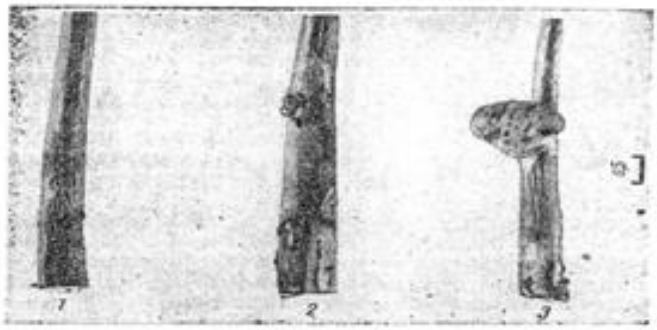
Fig.5 - 6. Different steps and growth of tumours on the roots of Indigoferatinctoria (Ergashev *et al.*, 2011; 2013; 20150)

Все штаммы, содержащие Ti-плазмиды с октопиновыми генами, вызывали опухоль на стеблях у вида G. hirsutum L. и оказались индифферентными при взаимодействии с видом G. barbadense L.:

Штаммы бактерий	Количество растений с опухолью на стебле* у вида хлопчатника G. hirsutum L.	Производные аргинина, синтезируемые в клетках опухолевой ткани
8933	0	Нопалин
8934	0	
C-58	0	
B_1	4	Октопин
2835	5	
B_6	>1	
1000	>4	
1058	4	
8628	>5	
Контроль	0	-

* При учете количества зараженных растений пользовались пятибалльной системой оценки: 0—растения с опухолью отсутствуют; 5—только (>0 %) половина из всех обработанных растений имеют опухоль; 1—растения (<0 %) с опухолью на стебле и т. д. Растения вида G barbadense L. опухоли не имели.

Штаммы бактерий, имеющие Ti-плазмиды с нопалиновыми генами, не вызывали образования опухолей у обоих видов хлопчатника.



Образование опухолевой ткани у растений хлопчатника вида G. hirsutum L., индуцированной A. tumefaciens, представлено на рисунке (где *1* — контроль, *2*, *3* — начальная и поздняя стадии развития

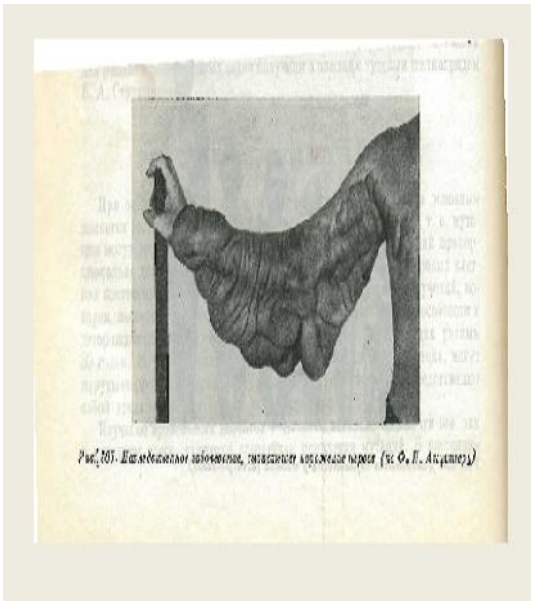
Fig. 7. Inducing of tumour by Ti-plasmid of A. tumefaciens in cotton plant steam (Ergashev *et al.*, 1983)

Fig. 8. The bacteria at the time of transfer of plasmids

Fig. 9 and 10. The tumour formation in Chinar (Eastern sycamore) and Oak

Fig. 11. Tumourgenesis in rosehip

Fig. 12. Tumorgenesis in cherri tree



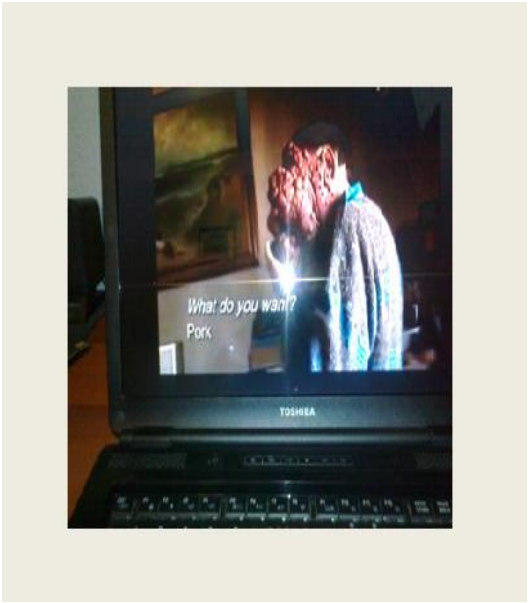


Fig. 13 and 14. The human tumour genesis

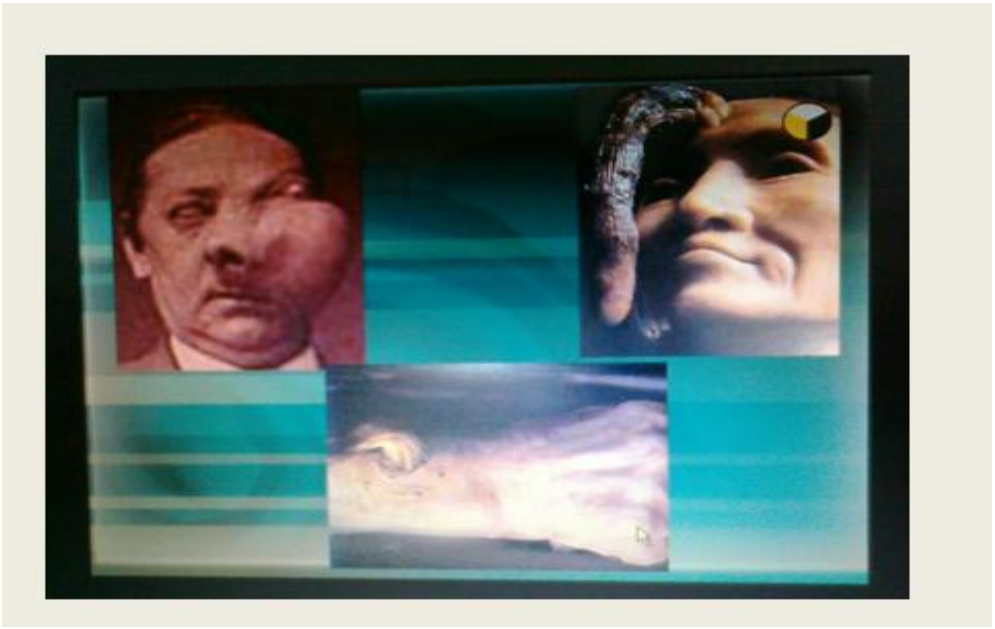


Fig.15. Plant genes can function in cells of the human body

A strong imbalance of nitrogen in nature in the last century, especially in the human environment, can provoke intensification and acceleration of the growth of tumour cells in all eukaryotes, including human. It is clear that bacterial genome, in terms of evolution, is more ancient than the eukaryotic genome, which are considered to be higher organisms. This means the cancer cell underlay the emergence of life on Earth since the dawn of evolution. In other words, it is likely that the very first Mother cell, which appeared billions of years ago, was a "tumour" cell. Here are some arguments in favour of this view. In order to evolve, the first cell had to constantly divide and acquire the ability to capture as much atoms of nitrogen as possible from a single source - the air, which at that time consisted mainly of nitrogen. Furthermore, the increased demand and supply of a sufficiently large number of nitrogen molecules for the synthesis of amino acids and proteins (enzymes), particularly nitrogenous bases of nucleic acids, accelerated this process without which neither a division or multiplication of cells would be possible. This was the main feature of tumour cells that differs from a normal one. Observations suggest that this is what has happened in the last decades in all areas of the Earth. To test the hypotheses, which are underlined as the basis of the above approach, one can use the mechanism of blocking of the enzyme activity-thimidilatsynthetase in tumour cells of eukaryote. It inhibits the DNA synthesis of the total cell genome, which then stops the cell from transition into the phase of G2 and mitotic division cycle. This can be achieved by using low-molar solution of 5-fluoro-2'-dezoxyuridine. Some pictures from different

source of authors are also attached, which can be useful for future research to find a trigger in understanding and treating this complex and overarching problems of modern biomedical and social science – the spread of cancer.

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