DESCRIPTION FOR THE GENERAL PUBLIC

Presently, there are many deadly or chronic diseases that pay special attention of scientists. However, the most serious among them is a negative mutation in cellular DNA, changing our own tissues into uncontrolled and self-existing formation called cancer. The dramatic effects carried by cancer are even more striking as it afflicts not only human, but endangered species or economically important breeds as well, pose social and economic thread to modern society. Let's assume that every single cell in living organism has the same chance to turn into mutated alien body. We can also agree that the probability of getting cancerogenic mutation increase with every consecutive cell division as double strains DNA need to be split and precisely rebuilt into two, exactly the same copies. If so, it is easy to predict that more cells the body have and longer it lives (more cell division will occur), it should have greater chance to develop cancer than smaller –short live organisms. Following that idea, for example whales weighting more than 100 tones and live nearly 100 years should have thousand times more negative mutations than weighting 20 grams and living around a year house mouse. However to date, scientists failed to confirm any relation between cancer incidences, body mass (i.e. cell number) and longevity. The surprising lack of correlation between body size (number of cells) and cancer risk across taxa is dubbed Peto's paradox. Interest in Peto's paradox resurges after it has been postulated that its solution can provide new methods of cancer prevention and treatment. Although, through the last couple of years tremendous progress in the field of genetics and cell biology has been made, a fully understanding of specific evolutionary mechanisms influencing the initiation and cancer development still remains far from the end.

Presently, the sole part of scientific studies concern cancers have been almost exclusively carried out on simplified animal models. While cancer is a compound disease, with many genes and proteins involved in its progression, such attempts cannot bring a particular progress. Interestingly, the latest model proposed to solve Peto's paradox suggests, that irrespective of body mass (and so the cell number), the differences in cell sizes, cell division rate, and/or metabolic rates between organisms may stand for the solution of this clue. Interdisciplinary, combined approach of evolutionary ecology, genetics, and medicine can shade then a new light on our understanding of cancer causes and the way it does develop. A strong test of the suggested association between metabolic rates, cells size and chance for cancer initiation should be provided by artificial selection experiments, which allow for manipulation between selected organismal traits directly related to the cancer. A novel study with the use of mice (as a model system) long-term selected for high and low basal metabolic rate (BMR) while body mass remains unaffected, constitute reasonable test for above predictions. Furthermore, apart from differences in BMR, proposed animals differ distinctly with the relative sizes of cells building the organism, as well as other, BMR-related traits as the ability to immune respond and susceptibility to toxicity – all with a possible impact on the rate of cells exhaustion, and so cancer probability. Thus, with the use of such model, it would be possible to control for additional variability influencing cancer incidence, which cannot be explain by body mass (cell number) alone as suggested in original concept of Peto's paradox. Moreover, it has been found that proposed selection for high and low BMR enforced multidirectional changes in cellular structure of metabolically important tissues. For example, the cells originated from organs belong to digestive systems as liver hepatocytes, kidney proximal tubule cell, and intestine enterocytes are considerably smaller in mice characterized by low basal metabolic rate, while their erythrocytes or skin epithelium cells remain bigger in compare to their cousins from high BMR line. As the size of cells strongly influences number and the rate of cell divisions, it is intriguing to check if the chance for cancer initiation varies in those tissues between each of selected BMR lines. This between line variation in cellular composition as well as differences in basal metabolic rate allow then for cross testing of influence of cell size, cell division rate, and metabolism on probability of cancer development, independently for each particular trait.

Aforementioned project, based on liver and skin cancer inductions in animals differ with respect to their metabolism rate, would has multidirectional cognitive aspects. First of all, it will determine whatever the rate of organismal metabolism has considerable influence on cancer initiations. Secondly, it should answer if small, short live and highly dividing cells are more prone to cancer development then larger ones. Thirdly, it would test if differences in basal metabolism of an organism are related to variation of selected molecular components (IGF, PDGF, p,27, p53, Akt/mTOR, Wnt/APC/β-catenin, Ras/myc) contribute in both, metabolic and cancer-related processes. The complex analysis from genomic level via cellular architecture to organismal metabolism should answer about the evolutionary mechanisms influencing cancer initiation and determining its progression. Such an innovative approach may provide straightforward explanation of the paradigm of Peto's paradox.