LETTER to the EDITOR

Possible Cancer Formation Mechanisms - View at the Cellular Level

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Dear Editor

The main theory behind cancer formation is that toxic substances, heavy metals, radiation (Davis et al., 2013), ultraviolet rays (Agrawal et al., 2013) and other physical and chemical stimuli cause genetic mutations, turning normal cells into cancer cells (Benigni and Bossa, 2011). Furthermore, with certain family genetic characteristics or genetic deficiencies, there is a higher possibility for normal cells to become cancer cells. Therapeutic cancer research has long strived to seek cancer drugs, most of which target cancer specific gene expression (Brannon-Peppas and Blanchette, 2004). However, after many decades of research with an enormous amount of research resource used throughout the world, cancer still remains incurable that cancer treatment could only extend patient's life rather than cure the disease. Perhaps there is still more to discuss other than the current theory. This study proposes a new theory of cancer formation that may help find the cure for cancer.

In the process of evolution, stress plays a crucial role in the survival of bio-organisms. Under extreme heat and coldness, toxic chemicals, radiation, ultraviolet rays or electromagnetic field, bio-organisms would have many responses, one of which is reproductive response. When a bio-organism is facing life-threatening stress, its reproductive response is triggered and accelerated to extend its life cycle.

For example, stress could stimulate blossom that has been found correlating to CO-like (COL) gene (Higgins et al., 2010; Kikuchi et al., 2012; Kitagawa et al., 2012). Treatment with ultrasound stress could stimulate bacterial growth (Pitt and Ross, 2003). The same phenomenon that stress could stimulate reproduction has also been observed on fish (Schreck, 2010), reptiles and birds Moore and Jessop, 2003; (Breuner et al., 2008). In comparison with normal cells, abnormal expression of reproductive and replicative genes such as CDT1, CDC6, FEN1 and POLD4 (Suzuki and Takahashi, 2013) have been found in cancer cells.

A single cell represents a unique and intact genome, and can be seen as an independent living organism as it can live in cell culture media. After several thousand to ten thousand years of evolution, in each cell, there are the genes and gene regulation, necessarily for surviving in stress during the evolutionary process. Therefore, response to stress can also be observed on cellular level. In response to stress, the gene expression required for cell growth and proliferation will be switched on, and that is called replication.

As to differentiated cells, they would possibly regulate gene expression for cell replication, in order to prolong their lifespan. When human cells are in contact with toxic substances, particularly when genes are attacked, cells will start proliferate by regulating gene expression for cell replication. This is one of the reasons of cancer formation, and it explains why many cancer drugs are able to inhibit cancer cell self-replication, but unable to cure cancer. Even when the replication of some cancer cells is inhibited by cancer drugs, the pathways of cell replication can be diverse that some uninhibited cancer cells would have other replicative ways once they enter the replicative state. This complicated process is the way cells try to cope with stress and survive. A known fact is that when cancer cells grow to a certain number, they will undergo self-gene regulation, due to lack of nutrients, and become metastatic cancer cells.

There are many carcinogenic factors and stresses for human. They may not be easily eradicated completely, but as long as stress-induced cancer cell proliferation can be inhibited, there is the hope of finding critical indicators and methods to effectively prevent cancer.

References

Agrawal A, Shindell E, Jordan F, et al (2013). UV radiation increases carcinogenic risks for oral tissues compared to skin. *Photochem Photobiol*, **89**, 1193-8.

Benigni R, Bossa C (2011). Mechanisms of chemical carcinogenicity and mutagenicity: a review with implications for predictive toxicology. *Chem Rev*, **111**, 2507-36.

Brannon-Peppas L, Blanchette JO (2004). Nanoparticle and targeted systems for cancer therapy. *Adv Drug Deliv Rev*, **56**, 1649-59.

Breuner CW, Patterson SH, Hahn TP (2008). In search of relationships between the acute adrenocortical response and fitness. *Gen Comp Endocrinol*, **157**, 288-95.

Davis DL, Kesari S, Soskolne CL, et al (2013). Swedish review strengthens grounds for concluding that radiation from cellular and cordless phones is a probable human carcinogen. *Pathophysiology*, **20**, 123-9.

Higgins JA, Bailey PC, Laurie DA (2010). Comparative genomics of flowering time pathways using Brachypodium distachyon as a model for the temperate grasses. *PLoS One*, **5**, e10065.

Kikuchi R, Kawahigashi H, Oshima M, et al (2012). The differential expression of HvCO9, a member of the CONSTANS-like gene family, contributes to the control of

flowering under short-day conditions in barley. *J Exp Bot*, **63**, 773-84.
Kitagawa S, Shimada S, Murai K (2012). Effect of Ppd-1 on the expression of flowering-time genes in vegetative and reproductive growth stages of wheat. *Genes Genet Syst*, **87**, 161-8.
Moore IT, Jessop TS (2003). Stress, reproduction, and adrenocortical modulation in amphibians and reptiles. *Horm Behav*, **43**, 39-47.
Pitt WG, Ross SA (2003). Ultrasound increases the rate of bacterial cell growth. *Biotechnol Prog*, **19**, 1038-44.
Schreck CB (2010). Stress and fish reproduction: the roles of allostasis and hormesis. Gen Comp Endocrinol, 165, 549-56.
Suzuki M, Takahashi T (2013). Aberrant DNA replication in cancer. *Mutat Res*, **743-744**, 111-7.

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