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Journal of Cancer Biology & Research

Case Report

Cancer: An Evolutionary Perspective

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Submitted: 25 June 2015

Accepted: 29 July 2015

Published: 31 July 2015

Keywords

- Cancer
- Evolution
- Natural selection
- Macro-mutation
- Atavism
- Antagonistic pleiotropy
- Cannibalism
- Contagious cancer

Abstract

Cancer is intricately linked to our evolutionary history. The origin and progression of cancer can hence be better understood when viewed from an evolutionary perspective. In this review, we portray the fundamental fact that within the complex ecosystem of the human body, the cancerous cells also evolve. Just like any organism, they face diverse selective pressure to adapt to the tumor environment. There exists a competitive struggle that eliminates the unfit, leaving the well-adapted to thrive. Sequential acquisition of "driver mutations", chromosomal instability triggering macro-mutations and punctuated bursts of genetic changes can all hypothetically contribute to the origin and evolution of cancer. We further describe that like in any ecosystem, cancer evolution involves not just the cancerous cells but also its interaction with the environment. However, as cancer evolves, individual cells behave more like a uni-cellular organism focused on its own survival. We also discuss evidences where cancer has evolved through transmission between individuals. An evolutionary analogy can open up new vistas in the treatment of this dreadful disease.

ABBREVIATIONS

COSMIC: Catalogue of Somatic Mutations in Cancer; AP: Antagonistic Pleiotropy; WBCs: White Blood Cells; DFTD: Devil Facial Tumor Disease; CTVT: Canine Transmissible Venereal Tumor

INTRODUCTION

Cancer is a disease where cells disobey normal growth control mechanisms leading to breakdown of homeostasis. However, the organized way they execute a definite cascade of changes and outwit the body's resistance defies random origin of cancer. In fact, inside all healthy individuals, there might be a dormant cancer program that can be turned on. The big question is what makes this switch to trip. Of late, scientists have tried to determine the evolving nature of cancer through various models to simplify the mechanism for development of appropriate therapeutic strategies in future [1,2]. Here, we analyze the possible set of events, from an evolutionary perspective that can induce cancerous features in a normal cell addressing the origin, complexity and dynamics of cancer.

Heterogeneity, the key to cancer evolution

The prevailing concept of stepwise cancer progression and its similarity to evolution was probably most convincingly described by Peter Nowell in 1976 in his theoretical paper in Science [3]. His proposal was novel for the time. Nowell suggested that the series of events taking place in cells progressing from normal to pre-cancerous to cancerous state represent a form of Darwinian evolution favored by natural selection. In the complex ecosystem of the human body, cells tend to accumulate mutations over time as they react to the changing tissue environment. Cells acquiring mutations or variations over several generations, that selectively favor aberrant growth and survival cause cancer. Each variant cancer cell can then further divide to form a clonal lineage, until the next genetic modification creates a new variant. Cancer is thus an outcome of repetitive clonal expansion, followed by clonal selection, in the adaptive tissue ecosystem. The result is a better adapted, heterogeneous tumor cell population [4,5]. More often than not, this evolutionary progression of cancer is abruptly terminated, or cancer preventive cellular mechanisms push back cancer to an old age. However, if the variant cell acquires early traits to evade the immune system and/or defy an apoptotic fate, cancer evolves fast and aggressively. In the context of the tumor environment, these defiant variants are thus the fittest. Extensive mutational heterogeneity has been described within tumors, with evidence of spatial intra-tumoral heterogeneity emerging in most solid tumors. In the seminal paper published in Science 2013, Kornelia Polyak and Andriy Marusyk, described the changes in the clonal dynamics of the population of cancer cells emphasizing on different identities in a single tumor population [6]. According to them, this heterogeneity allows tumors to deal with selective pressures. There is a probability that some cells empowered by specific genes will survive in a genetically diverse tumor, while millions of cells die upon exposure to a drug. When most cells are killed off —they continue to re-populate and re-establish the residual cancerous mass over time. Diverse genetic changes in the tumors thus reduce the efficacy of drugs and are probably the reason for refractoriness to anti-cancer agents [4, 5]. Therefore, understanding cancer should begin with identifying the critical

environmental pressures, corresponding adaptive cellular strategies and the subsequent evolution of the disease.

Cancer cell survival and evolution requires social networking

As discussed above cancer evolves amidst heterogeneity. Hence, we can assume a tumor as a "continent" inhabited by multiple cellular species that adapt to spatial variations. The more diverse the environment, the more heterogeneous the population, as observed in advanced tumors. Strikingly, cancer cells in the "continent" show social behavior in terms of communication to become better adapted in the system. They work in harmony with each other and attempt to fight the system. They can recruit surrounding non-cancerous cells which provide physical support and protect them from the immune system. In this respect, Prof. Donald Coffey describes cancer, as a group of smart communicating cells with unique characters for co-operative behavior. He emphasizes that cancer cells like bacteria can change their own environment for better survival. Like bacteria, they may swallow up their peers when they run out of resources, a phenomenon referred as cancer "cannibalism" [7]. The cannibalistic cancer cells may feed not only on their siblings, but also on lymphocytes that kill them. There are also instances where cancer cells have fused with immune cells, like macrophages [8]. German biologist Otto Aichel, way back in 1911, first proposed that cancer cells and white blood cells (WBCs) such as macrophages could fuse. The resultant hybrid cells can then have both the proliferative power of cancer and the migratory potential of WBCs [9]. A very recent report states that tumor cells can import mitochondrial DNA from normal host cells through horizontal transfer of mitochondrial genome in order to re-vamp respiration and proliferative efficacy [10]. Thus, understanding the communication code of cancer can motivate new research directions and lead to the development of novel therapies.

The ecological aspect of evolution

In the heterogeneous environment of tumors, the evolution of cancer can also be fully understood if viewed from an ecological perspective. One can imagine tumorigenesis as an attempt of newly emergent species, with different metabolic demands compared to the existing population. Therefore, it is conceivable that ecological factors like, competition, predation or parasitism can affect relative fitness of cancer cells. Competition can prevail in the form of resource utilization where different neoplastic clones can inhibit growth of the other [11,12]. Like parasites, neoplastic cells can benefit from their neighbors at no cost to themselves. They can rely on metabolic expenditure of their neighbors, such as stimulating fibroblasts to secrete growth factors, invite macrophages, feed on their secretion for their own growth advantage [13]. In 1990, G. H. Heppner and B. E. Miller showed that a malignant clone can induce an otherwise non-malignant clone with similar characters thus increasing fitness through commensal interactions [14]. Also, tumor–stroma exchange is a kind of commensalism, as the normal cells can support and even promote tumorigenesis. Robert Axelrod proposed that tumor cell clones can co-operate, and thereby thwart the requirement of acquiring all the hallmarks of cancer by a single clone [15,16]. He suggested that two cells in proximity can protect each other; and neither can live alone. Thus co-operation evolves amongst genetically diverse cells [17]. Moreover, for a cancerous cell to invade a tissue, the resident host cells must be off their adaptive peak [18, 19]. Aging probably is one such state in which host cells fall off of their adaptive peak inviting cancerous traits. Also, there are more chances of invasion when the ―host‖ population is specialized for the niche, whereas the intruders, as in metastatic cells are generalists— less efficient in some aspects, but capable of utilizing several resources [18,19]. Hence in 2008, Pienta introduced the term ecological therapy for cancer treatment where he emphasized that targeted obliteration of the tumor micro-environment might be a more effective strategy than indiscriminate carnage of cells [20].

Cancers can take giant leaps: the macro-evolutionary approach

Predicting cancer's move could well be the best strategy to eradicate it. We know that as cancer progresses, it has to accomplish several remarkable feats: first grow *in situ* and survive a harsh environment, segregate itself from the primary tumor; force through the wall of vessels; outsmart the immune system; and finally, re-establish at a new location. How does cancer achieve such a daunting task? Does one single cell go awry? Or do multiple cells accumulate changes over time to burst out of control? Interestingly, recent reports suggest that during tumorigenesis, rapid adaptation, marked by acquisition of advantageous traits, an increased mutation rate, and a rapidly evolving dynamic population size is often critical [21-23]. The traditional, Darwinian gradualist view fails to explain such dynamicity. Evolutionists are aware of it and admit that too; small-scale changes, such as, random mutations, probably do not provide the impetus or is too simplistic. Way back in 1940, biologist Richard Goldschmidt stated that organisms split into new species when large mutations incur in a single generation, forming a better-adapted organism, which he called "hopeful monster" [24]. Of late, Charles Swanton experimentally proved in solid tumors that cells can drastically re-order their genome, evolving abilities in large leaps to provide the thrust they need [25,26]. He proposes that chromosomal instability due to ―genome doubling‖ or copy number variations (CNVs) can generate ―macro-evolutionary leaps". Cells take these ―big genetic jumps‖ to acquire traits, even if, they might turn out to be unfit in the system. Cancer cells similarly, can gain and/or lose pieces of chromosomes at an alarming speed, creating the hopeful monsters [27].

Evolution defies the equilibrium between order and disorder

Considering that cancer does not follow a gradualist phenomenon, a school of biologist believes that cancer cells switch between punctuated and stepwise phases during their genome evolution [28,29]. The punctuated phase driven by chromosomal instability is characterized by massive genomic alterations. Contrarily, the stepwise phase is marked by gradual buildup of small genomic alterations. Studies in chronic lymphocytic leukemia show that cancer cells can occasionally experience catastrophic 'event termed chromothripsis, where the genome acquires a large number of re-arrangements which is

generally followed by a period of small scale changes [29]. During chromothripsis, hundreds to thousands of genomic modifications occur within restricted regions which can lead to multiple cancer-driving alterations [30]. The fact that cancer cells can endure this level of genetic re-shuffling implies a selective advantage for such an event. The punctuated equilibrium approach thus involves a transition from one equilibrium state to another, a shift from "order to disorder" and reiteration of it over time. What remains to reason out is why, in spite of evolution favoring an eventual increase in the entropy or disordered state favors order in the form of multi-cellularity? Future studies into these aspects can only help explain such behavior.

Tipping the balance between driver and passenger mutations

As we discuss genetic alterations guiding cancer evolution, it is worthwhile to point out that the course of cancer is often determined by a delicate balance between different types of mutations. Cancer requires rapid acquirement of new traits and hence a high mutation rate. The mutations that are helpful to cancer cells, as they increase proliferation rate or eliminate breaks on cell division are often termed as "driver mutations". Drivers, can arise together with hundreds of other mutations dispersed throughout the genome with no immediate effect, collectively termed as "passengers". Driver mutations are critical for cancer development; however, passenger mutations are generally considered inconsequential, benign and can evade natural selection [31]. Christopher McFarland in his 2014 PNAS paper argues on the un-explored importance of accumulation of passenger mutations in cancer. He emphasizes that it is actually the balance between driver and the load of passenger mutations that determines a cancerous fate [32]. The passenger mutations inhibit cancer progression restricted by a decisive population size, below which most cancers do not progress, and a critical mutation rate above which cancers degenerate [31,32]. If enough passenger mutations are present, their cumulative effect can slow a tumor growth. Also, if new driver mutations are acquired the growth can kick start again [32]. Under this situation, cancer cells must acquire rare mutations and yet shun mutational meltdown. This tells why most adaptive processes often fail. It also explains why only about 0.1% of pre-cancerous lesions ever proceed to cancer. To triumph over cancer, we should therefore understand the constraints evolution imposes on rapid adaptation.

Why then evolution favors cancer?

If the human genome is a product of evolution that involves natural selection, then why under selective pressure, evolution favors genes or its allelic variants with cancerous effects and not eliminates them by selection over time? It can be best explained through antagonistic pleiotropy (AP) hypothesis proposed by George Williams in 1957 [33]. It is thought to be one of the several reasons as to why organisms are not able to reach perfection through natural selection. According to this hypothesis, genes that are pleiotropic and control both beneficial as well as deleterious traits (AP), if persist in the course of natural selection, prevent organisms from reaching perfection. Precisely, if an organism harbors the benefits of a gene, they also own the burden of its faults. This also applies to the allelic variants of genes which arise due to mutations; where some mutations improve the gene's function from one aspect, but, simultaneously causes a harmful effect from another aspect. For example, variation in "CAG" tri-nucleotide repeat lengths within the androgen receptor (AR) gene, in males and females, exhibits similar AP effect. In females, a shorter repeat length (SRL) increases reproductive ability and reduces breast cancer risk; while paradoxically, it is associated with increased risk of ovarian cancer later in life (SRL is associated with enhanced expression of AR gene in ovarian tissues). Again, in males, SRL is associated with increased reproductive fitness and reduced risk of Kennedy's disease; but also with increased mortality due to prostate cancer (mostly at an old age) [34]. Evolutionary biologist like, Peter Medawar suggests that the force of natural selection dwindles with increasing age [35,36]. Hence, selection is unable to spoil the deleterious effects of genes/allelic variants when expressed at advanced ages. Considering that cancer is predominantly an old age disorder, alleles can exhibit AP effects depending on whether the selection is strong or weak. Genes that exhibit beneficial effects on fitness early in life, when selection is strong, can have a cancerous effect later in life, when the selection is weak. Under the umbrella of evolution, we believe that AP best explains the uncontrolled behavior of cancer cells.

Cancer shows characters like uni-cellular organisms

Cancer cells are often viewed from a "single cell" perspective irrespective of the multi-cellular organism, its host. In 1911, in a paper published in British Medical Journal, Sir Henry Butlin proposed that cancer cells are - —nearest to the protozoa-so near, indeed, that it is difficult to keep it out of the protozoa‖. He named the cancer cells as "unicellular cancri" – protozoa like organisms [37]. Protozoans are single-celled organisms commonly with animal like behavior. Well, millions of years ago, virtually all living creatures were single-celled and every cell used to live for itself; cancer was probably non-existent. Also, unrestrained multiplication of uni-cellular organisms was not something atypical. With evolution, things changed; single-cell creatures learned co-operation, enjoyed the fruits of togetherness, and that lead to the evolution of multi-cellularity. Unlike uni-cellular organisms, cells in multi-celled organisms are specialized to perform definite functions. In order to promote the fitness of the whole organism individual cells' proliferative potential is restricted, and the job to pass on the traits to next generation is outsourced to gametes. When a single cell defies this collective imperative and reverts to the old habit of proliferating aggressively, only for its own survival and propagation- that is what we call cancer. Cancer is often considered as an independent organism with completely new traits and uni-cellular like behavior evolved from multi-cellular life forms [38].

The limits to evolution of cancer

Is there a limit to cancer's ability to evolve? We frankly do not have an answer yet. Evolutionary biologist, Julian S. Huxley suggested that cancers probably occupy a completely different clade in the tree of life with respect to its hosts [39]. Professor Peter Duesberg further states that due to acquisition of huge chromosomal instability cancer cells acquire totally new characteristics and an unpredictable genotype distinct from the host or parental cells that they originated from [40,41]. The

metastatic cancer cells are even more deviated not only from the parental cell types but also harbor features different from one another. Consider the example of HeLa cells which were isolated in 1951 from a cervical cancer patient. The cells are still growing robustly outside the body of the host, and have probably attained immortality by now. In 1991, biologist Van Valen, proposed something very radical when he raised the question whether HeLa cells do any longer possess genotype close to humans? He pointed out that the genetic material of these cells has undergone major variations and are far outside the range of any healthy human being. He consequently suggested a scientific name for HeLa cells, *Helacyton gartleri* [42]. We believe that this proposition where carcinogenesis meets speciation will lead to new approaches treating cancer. In fact, Dr. Vincent suspects that cancer cells operate right at the edge of survivability, maintaining genomic flexibility, yet holding on to the ability to divide and hence, motivating them to evolve even faster can be an appropriate strategy to knock them off [38].

Cancer as a transmissible disease

In the year 2006, Anee Pearse was probably the first to postulate that cancer can spread and evolve [43]. Cancer was never thought to be contagious before, but growing evidences suggest that cancer cells can break free from their host, self-sustain and infect other organisms. An example is the Tasmanian devil facial tumor disease (DFTD). This disease probably originated in a single devil and then spread, in spite of arising separately within each animal. Tumors from several devils were found to have strikingly similar chromosomal pattern, but were genetically distinct from their hosts [44, 45]. DFTD became contagious probably by turning off the major histocompatibility complex (MHC) genes [46]. Another example of clonally transmissible cancer is canine transmissible venereal tumor (CTVT). It is speculated that CTVT first originated in wolves and then spread to dog. The striking similarity between DFTD and CTVT is that they both didn't die off with their host, but found ways to invade a new host and sustain themselves [47]. DFTD and CTVT are currently the only known contagious cancers to be reported. Naturally occurring contagious cancer is rare; however, its rate of occurrence may well be underrated till date. Fortunately, there isn't any naturally transmittable cancer in human, not that we know of yet, however, it is difficult to speculate when one is going to evolve.

DISCUSSION AND CONCLUSION

Cancer is a disease that is common to plants and animals, as well as humans. It must have evolved millions of years ago when we all shared a common ancestor. At that point of time, cells were probably more benefitted by unrestrained proliferation, as cancer does, and higher functionality of cells was not much required. With evolution of multi-cellular organisms with large bodies, complexity of function and long lives we probably developed mechanisms to limit un-inhibited proliferation of cells or cancer. Cancer is probably a breakdown of this higher protective functionality of cells. Also, cancer development within a single individual organism follows an evolutionary trajectory - from acquisition of mutations, to formation of initial tumor, to development of a metastatic monster in many aspects do mirror species evolution. Hence, looking for evolutionary cues to a complex disease like cancer can not only help us to better understand the disease, but can also provide clues to develop more rational novel therapeutic approaches.

ACKNOWLEDGEMENTS

We thank BITS-Pilani for providing us support to continue cancer research & our lab members 'Subhra Dash and Sukalpa Mondal for continuous discussions and debates over the topic.

REFERENCES

1. Gatenby RA, Vincent TL. Application of quantitative models from population biology and evolutionary game theory to tumor therapeutic strategies. Mol Cancer Ther. 2003; 2: 919-927.
2. Maley CC, Reid BJ, Forrest S. Cancer prevention strategies that address the evolutionary dynamics of neoplastic cells: simulating benign cell boosters and selection for chemosensitivity. Cancer Epidemiol Biomarkers Prev. 2004; 13: 1375-1384.
3. Nowell PC. The clonal evolution of tumor cell populations. Science. 1976; 194: 23-28.
4. Gillies RJ, Flowers CI, Drukteinis JS, Gatenby RA. A unifying theory of carcinogenesis, and why targeted therapy doesn't work. Eur J Radiol. 2012; 81 Suppl 1: S48-50.
5. Gillies RJ, Verduzco D, Gatenby RA. Evolutionary dynamics of carcinogenesis and why targeted therapy does not work. Nat Rev Cancer. 2012; 12: 487-493.
6. Marusyk A, Polyak K. Cancer. Cancer cell phenotypes, in fifty shades of grey. Science. 2013; 339: 528-529.
7. Ben-Jacob E, Coffey DS, Levine H. Bacterial survival strategies suggest rethinking cancer cooperativity. Trends Microbiol. 2012; 20: 403-410.
8. Sharma N, Dey P. Cell cannibalism and cancer. Diagn Cytopathol. 2011; 39: 229-233.
9. Ding J, Jin W, Chen C, Shao Z, Wu J. Tumor associated macrophage × cancer cell hybrids may acquire cancer stem cell properties in breast cancer. PLoS One. 2012; 7: e41942.
10. Tan AS, Baty JW, Dong LF, Bezawork-Geleta A Endaya B, Goodwin J, et al. Mitochondrial genome acquisition restores respiratory function and tumorigenic potential of cancer cells without mitochondrial DNA. Cell Metab. 2015; 21: 81-94.
11. Guba M, Cernaianu G, Koehl G, Geissler EK, Jauch KW, Anthuber M, et al. A primary tumor promotes dormancy of solitary tumor cells before inhibiting angiogenesis. Cancer Res. 2001; 61: 5575-5579.
12. Miller BE, Miller FR, Leith J, Heppner GH. Growth interaction in vivo between tumor subpopulations derived from a single mouse mammary tumor. Cancer Res. 1980; 40: 3977-3981.
13. Seliger B. Strategies of tumor immune evasion. BioDrugs. 2005; 19: 347-354.
14. Miller FR, Heppner GH. Cellular interactions in metastasis. Cancer Metastasis Rev. 1990; 9: 21-34.
15. Roberts. Malignancy and Evolution. 1926.
16. Snow. Cancers and the Cancer Process.1893.
17. Axelrod R, Axelrod DE, Pienta KJ. Evolution of cooperation among tumor cells. Proc Natl Acad Sci U S A. 2006; 103: 13474-13479.
18. De Gregori J. Evolved tumor suppression: why are we so good at not getting cancer? Cancer Res. 2011; 71: 3739-3744.
19. Tilman D. Niche tradeoffs, neutrality, and community structure: a

stochastic theory of resource competition, invasion, and community assembly. Proc Natl Acad Sci USA. 2004; 101: 10854-10861.

20. Pienta KJ, McGregor N, Axelrod R, Axelrod DE. Ecological therapy for cancer: defining tumors using an ecosystem paradigm suggests new opportunities for novel cancer treatments. Transl Oncol. 2008; 1: 158-164.

21. Berger MF, Hodis E, Heffernan TP, Deribe YL, Lawrence MS, Protopopov A, et al. Melanoma genome sequencing reveals frequent PREX2 mutations. Nature. 2012; 485: 502-506.

22. Beroukhim R, Mermel CH, Porter D, Wei G, Raychaudhuri S, Donovan J, et al. The landscape of somatic copy-number alteration across human cancers. Nature. 2010; 463: 899-905.

23. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011; 144: 646-674.

24. Dietrich MR. Richard Goldschmidt: hopeful monsters and other 'heresies'. Nat Rev Genet. 2003; 4: 68-74.

25. Birkbak NJ, Eklund AC, Li Q, McClelland SE, Endesfelder D, Tan P, et al. Paradoxical relationship between chromosomal instability and survival outcome in cancer. Cancer Res. 2011; 71: 3447-3452.

26. Roylance R, Endesfelder D, Gorman P, Burrell RA, Sander J, Tomlinson I, et al. Relationship of extreme chromosomal instability with long-term survival in a retrospective analysis of primary breast cancer. Cancer Epidemiol Biomarkers Prev. 2011; 20: 2183-2194.

27. Heselmeyer-Haddad, K, Berroa Garcia LY, Bradley A, Ortiz-Melendez C, Lee WJ, Christensen R, et al. Single-cell genetic analysis of ductal carcinoma in situ and invasive breast cancer reveals enormous tumor heterogeneity yet conserved genomic imbalances and gain of MYC during progression. Am J Pathol. 2012. 181: 1807-1822.

28. Heng HH, Stevens JB, Liu G, Bremer SW, Ye KJ, Reddy PV, et al. Stochastic cancer progression driven by non-clonal chromosome aberrations. J Cell Physiol. 2006; 208: 461-472.

29. Stephens PJ, Greenman CD, Fu B, Yang F, Bignell GR, Mudie LJ, et al. Massive genomic rearrangement acquired in a single catastrophic event during cancer development. Cell. 2011; 144: 27-40.

30. Wyatt AW, Collins CC. In Brief: Chromothripsis and cancer. J Pathol. 2013; 231: 1-3.

31. McFarland CD, Mirny LA, Korolev KS. Tug-of-war between driver and passenger mutations in cancer and other adaptive processes. Proc Natl Acad Sci U S A. 2014; 111: 15138-15143.

32. McFarland CD, Korolev KS, Kryukov GV, Sunyaev SR, Mirny LA. Impact of deleterious passenger mutations on cancer progression. Proc Natl Acad Sci U S A. 2013; 110: 2910-2915.

33. Williams GC. Pleiotropy, Natural selection, and the evolution of senescence. Evolution. 1957; 11: 398-411.

34. Carter AJ, Nguyen AQ. Antagonistic pleiotropy as a widespread mechanism for the maintenance of polymorphic disease alleles. BMC Med Genet, 2011. 12: 160.

35. Haldane JBS. New paths in genetics. 1941 London: G. Allen & Unwin ltd. 2 pl, 7-206 p.

36. Medawar PB. An unsolved problem of biology. London: Published for the college by H. K. Lewis. 1952, 24 p.

37. Butlin H. Two Lectures ON UNICELLULA CANCRI: THE PARASITE OF CANCER: Delivered before the Royal College of Surgeons of England. Br Med J. 1911; 2: 1457-1461.

38. Vincent M. Cancer: a de-repression of a default survival program common to all cells: a life-history perspective on the nature of cancer. Bioessays. 2012; 34: 72-82.

39. Huxley J. Cancer biology: comparative and genetic. Biol Rev 1956. 31: 474-514

40. Duesberg P, Iacobuzio-Donahue C, Brosnan JA, McCormack A, Mandrioli D, Chen L. Origin of metastases: subspecies of cancers generated by intrinsic karyotypic variations. Cell Cycle. 2012; 11: 1151-1166.

41. Duesberg P, Mandrioli D, McCormack A, Nicholson JM. Is carcinogenesis a form of speciation? Cell Cycle. 2011; 10: 2100-2114.

42. Van Valen, LMA.VCM. HeLa a new microbial species. Evolutionary Theory, 1991. 10: 71-74.

43. Pearse AM, Swift K, Hodson P, Hua B, McCallum H, Pyecroft S, Taylor R. Evolution in a transmissible cancer: a study of the chromosomal changes in devil facial tumor (DFT) as it spreads through the wild Tasmanian devil population. Cancer Genet. 2012; 205: 101-112.

44. Murchison EP, Tovar C, Hsu A, Bender HS, Kheradpour P, Rebbeck CA, et al. The Tasmanian devil transcriptome reveals Schwann cell origins of a clonally transmissible cancer. Science. 2010; 327: 84-87.

45. Murchison EP, Wedge DC, Alexandrov LB, Fu B, Martincorena I, Ning Z, et al. Transmissible [corrected] dog cancer genome reveals the origin and history of an ancient cell lineage. Science. 2014; 343: 437-440.

46. Siddle HV, Kreiss A, Tovar C, Yuen CK, Cheng Y, Belov K, et al. Reversible epigenetic down-regulation of MHC molecules by devil facial tumour disease illustrates immune escape by a contagious cancer. Proc Natl Acad Sci U S A. 2013; 110: 5103-5108.

47. McCallum H. Tasmanian devil facial tumour disease: lessons for conservation biology. Trends Ecol Evol. 2008; 23: 631-637.

Cite this article

Nagraj J, Mukherjee S, Chowdhury R (2015) Cancer: An Evolutionary Perspective. J Cancer Biol Res 3(2): 1064.