

Cancer Treatment 2020- Stem Cell Versus The De-De-Differentiation Hypotheses Of Human Carcinogenesis: Adult Human Organ-Specific Stem Cells As Targets For Cancer Stem Cells

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Abstract:

Human Carcinogenesis appears to fit the “*Initiation*”, “*Promotion*”, “*Progression*” concept, that involves multiple steps and mechanisms. The two major, but opposing, hypotheses of the origin of this process, by which one normal cell is “initiated” to start this complex evolutionary process, include the “*stem cell*” hypothesis and the “*de-differentiation*” or “*Re-programming*” hypotheses. With the isolation of human stem cells (embryonic and organ specific adult stem cells), as well as the “induced pluripotent stem cells” (“iPS”), arguments have been made to support both competing hypotheses.

The basic assumption to be made in this presentation is that there appears to be more direct evidence to support the hypothesis. Since every human organ contains organ-specific adult stem cells, a single rare normal adult stem cell can be converted from a cell capable of either symmetrical or asymmetrical cell division to one that can not divide asymmetrically, by an “*Error-Prone DNA Repair*” Process or by an “*Error Prone DNA Replication*” process, to become “initiated”. This single “initiated” adult organ-specific stem cell, if exposed to “epigenetic agents”, such as pollutants, drugs, cytokines, hormones, growth factors, at threshold levels, for regular and sustained fashion, in the absence of antioxidants, can be “promoted” to become independent of these promoters and to be transformed to an invasive and metastatic “cancer stem cells”.

Evidence will be presented from the isolation and characterization of a human breast adult stem cell, having expressed *Oct4A*, *ABCG-2* genes, but having no expressed *Connexin* genes or having no function *gap junctions*. These cells will be shown to give rise to

human breast cancer stem cells. Moreover, these normal or “cancer stem cells” will be shown to form 3-D organ-specific “organoids” that can be used to screen for both tumor promoters or chemo-preventive agents.

Professional Biography: James E. Trosko completed his PhD at the age of 25 years from Michigan State University and spent 3 years as a postdoctoral fellow at Oak Ridge National Laboratory under Drs. Ernest Chu; Dr. Sheldon Wolff and Dr. Richard Setlow. After joining Michigan State University, he obtained an NCI- Career Development award; spent one year at the McArdle Lab for Cancer Research at the University of Wisconsin under Dr. Van R. Potter. Later, he was Chief of Research at the Radiation Effects Research Foundation for two years in Hiroshima and Nagasaki, Japan. He spent 2 years at Seoul National University as a Korean “World Class University Professor”. He also spent one year at the ARNAS-Civico-Regional Cancer Hospital in Palermo, Sicily. He is currently an MSU-Distinguished Emeritus Professor. He has published more than 450 papers.

Presentation: The job of undifferentiated organisms to keep up the “condition of everlasting status” in a “mortal multicellular being”

While it may be contended that a solitary cell life form, for example, a bacterium, is an unfading cell, over the span of natural advancement, new phenotypes rose that gave endurance favorable circumstances when cells composed into a firm society of cells to shape a multi-celled creature. While temperature, accessibility of supplements, pH, environmental elements, and radiation impacted the development guideline of these single cell living beings, strength for the

species was kept up by the hereditary data that secured by a moderately blunder free DNA fix and DNA replication framework. The single cell life form species endure the inescapable changes of condition, in which it got itself, basically by having the option to multiply by means of a balanced cell division to accomplish a huge populace, in which just a couple of transformations happened, bearing on its capacity to endure another condition. In the multi-cell living being, a "Faustian deal", of sorts, was made for new versatile highlights that permitted this assortment of firm cells to get by to keep up the species. Obviously, while the vast majority of the components that controlled cell development of the single cell life form are pertinent for the individual cells of the multi-cell life form, inner or endogenous development control was expected to direct the numerous cells inside the multi-cell living being. Also, a few cells surrendered standard "self replication" capacity so as to give exceptionally specific versatile capacity to the endurance preferred position of the entire living being. Therefore, the procedure of "separation" showed up, along with the component that permitted "awry cell division" to enhance the procedure of even cell division. This novel element of a cell's capacity to multiply either by balanced cell division (to expand the cell quantities of like-type cells) or by deviated cell division (to keep up homeostatic degrees of little girl like mother cell however to permit the arrangement of a separation of a specific cell) is a "trademark" of a multi-cell metazoan. What's more, as a result of this separation procedure was the acceptance of "mortality" of both the particular separated cell and eventually, the entire life form. An exceptional type of cell passing, customized cell demise or apoptosis likewise created the impression that supported in permitting the multi-cell living being to obtain new versatile highlights. The change of the single cell, treated egg to a hatchlings, pupae and butterfly, for instance, required particular cells at each period of advancement (food obtaining qualities/phenotypes) to offer approach to fresher specific cells that eventually gave the finished result of improvement of wing muscles for a grown-up

butterfly to mate, and give the qualities to keep up the species.

Plainly, while practically all the phones of the multi-cell living being contain the all out genomic data of the species, just a bit of those qualities are communicated in each specific cell. Along these lines, the procedure to direct, effectively, explicit battery of qualities from the complete genome more likely than not rose during this transformative progress from the single cell organ to the multi-cell life form.

All together that the individual, mortal, multi-cell creature help to keep up the endurance of the species to which it had a place, the arrangement of both germinal stem and physical or grown-up foundational microorganisms was required. The relative genomic soundness must be kept up in the germ undeveloped cells, with periodic transformations happening, to give the species a supply of new hereditary choices to adjust to the unavoidable ecological changes. Found as such, the multi-cell creature's germinal foundational microorganisms were eternal, while the human individual was just the transient transporter for these interminable undifferentiated cells.

The physical undeveloped cell additionally rose during this transformative progress from the single cell "undying" life form to the human individual multi-cell living being that conveyed eternal germ cells. So as to go through its different improvement stages (incipient organism, hatchling, neonate, youthful, develop and geriatric stages), procedures to give the entire living being sufficient cells for development, separation, just as for wound-recuperating and demise because of apoptosis, needed to rise. The improvement of a one of a kind sort of immature microorganism, which had the capacity to self-restore (the two little girl cells having held the capacity be an undeveloped cell as the mother cell), just as to isolate

lopsidedly for the creation of one little girl to keep up "stemness", including looking after everlasting status, and the other to be a 'travel intensifying" cell, resolved to have a limited life expectancy that could separate, senescence or apoptosis.

In contemporary terms, there is by all accounts various undeveloped cell types. The "toti-powerful" undifferentiated organism is the treated egg, which means it can offer ascent to all cell types (around 200 on account of the person) and the repeating individual with both the germinal and physical foundational microorganisms. The germinal immature microorganism can give rise, at last, to either sperm or eggs. It dwells in its extraordinary specialty (1). As the incipient organism begins to frame from the treated egg, (blastomere, gastrula, and so forth (2)), the toti-strong immature microorganism begins to limit the little girl undifferentiated organisms' capacity to offer ascent to an entire individual, yet keeps up the capacity to offer ascent to the various substantial cell types. These are "pluri-strong" undifferentiated cells. As the undeveloped organism travels to the fetal stage, the smaller scale ecological changes, which, more then likely, gives various signs to control various qualities to adjust to this new circumstance. Showing this excellent robotic connection between specifically directing explicit qualities out of the all out genome by a falling self-prompting grouping as advancement continues is the depiction of this procedure

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