

# 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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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 hypothesis. 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 3D organ-specific organoids that can be used to screen for both tumor promoters and chemo-preventive agents.

## Introduction:

The job of undifferentiated organisms to keep up the "condition of interminability" in a "mortal multicellular being"

While it may be contended that a solitary cell life form, for example, a bacterium, is an eternal cell, throughout natural advancement, new phenotypes developed that gave endurance preferences when cells sorted out into a strong society of cells to frame a multi-celled life form. While temperature, accessibility of supplements, pH, climatic components, and radiation affected the development guideline of these single cell living beings, soundness for the species was kept up by the hereditary data that ensured by a generally mistake 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 strong cells to make due to keep up the species. Obviously, while the greater part of the elements that controlled cell development of the single cell living being are pertinent for the individual cells of the multi-cell creature, inner or endogenous development control was expected to direct the numerous cells inside the multi-cell living being. Besides, a few cells surrendered conventional "self replication" capacity so as to give exceptionally specific versatile capacity to the endurance bit of leeway of the entire living being. In this way, the procedure of "separation" showed up, along with the component that permitted "deviated cell division" to enhance the procedure of balanced cell division. This one of a kind element of a cell's capacity to multiply either by balanced cell division (to expand the cell quantities of like-type cells) or by topsy-turvy cell division (to keep up homeostatic degrees of little girl like mother cell yet to permit the arrangement of a separation of a particular cell) is a "trademark" of a multi-cell metazoan. Also, as a result of this separation procedure was the enlistment of "mortality" of both the particular separated cell and at last, the entire life form. An extraordinary type of cell demise, customized cell passing or apoptosis likewise gave the idea that helped in permitting the multi-cell life form to obtain new versatile highlights. The progress of the single cell, treated egg to a hatchlings, pupae and butterfly, for instance, required particular cells at each period of improvement (food procuring qualities/phenotypes) to offer approach to more up to date concentrated cells that at last gave the final result of advancement 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 life form contain the absolute genomic data of the species, just a segment of those qualities are communicated in each specific cell. In this way, the procedure to direct, accurately, explicit battery of qualities from the all out genome more likely than not rose during this developmental progress from the single cell organ to the multi-cell creature.

All together that the individual, mortal, multi-cell living being help to keep up the endurance of the species to which it had a place, the arrangement of both germinal stem and substantial or grown-up undifferentiated organisms was required. The relative genomic dependability must be kept up in the germ foundational microorganisms, with infrequent transformations happening, to give the species a store of new hereditary choices to adjust to the inescapable natural changes. Found as such, the multi-cell life form's germinal undifferentiated organisms were unfading, while the human individual was just the transient bearer for these undying immature microorganisms.

The physical undeveloped cell likewise rose during this transformative change from the single cell "undying" living being to the human individual multi-cell living being that conveyed unfading germ cells. So as to go through its different improvement stages (incipient organism, hatchling, neonate, juvenile, develop and geriatric stages), procedures to give the entire life form enough cells for development, separation, just as for wound-mending and demise because of apoptosis, needed to rise. The advancement of an extraordinary kind of immature microorganism, which had the capacity to self-restore (the two 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 undifferentiated cell types. The "toti-strong" 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 recreating individual with both the germinal and substantial immature microorganisms. The germinal undifferentiated organism can give rise, at last, to either sperm or eggs. It lives in its exceptional specialty . As the incipient organism begins to shape from the prepared egg, (blastomere, gastrula, and so on , the toti-intense foundational microorganism begins to confine the girl undifferentiated cells' capacity to offer ascent to an entire individual, yet at the same time keeps up the capacity to offer ascent to the various substantial cell types. These are "pluri-intense" foundational microorganisms. As the undeveloped organism travels to the fetal stage, the miniaturized scale ecological changes, which, no doubt, gives various signs to manage various qualities to adjust to this new circumstance. Delineating this excellent computerized connection between specifically managing explicit qualities out of the all out genome by a falling self-prompting arrangement as advancement continues is the depiction of this procedure by C. Markert