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Mini Review

Current Conundrums: How Malleable is Today's Icon of Stem Cell Focus?

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Abstract

As important as it is to embrace the twist of events in our rapidly evolving world, it becomes essentially relevant to project the current roadblocks encountered in regenerative medicine and its potential applications, most specifically, the stem cell engineering focus. There has been an undoubted progress in this field while the scientific cellular manipulations in engineering efforts have been well controlled to meet ethical standards to near satisfaction. Nevertheless, there are still hurdles encountered in the field regarding efficiency and the limitation of its clinical applications even though outcomes can be appreciated at the experimental frame.

This letter therefore aims to shed valuable insights into where the current stem cell maneuvers and technology are potentially headed in regard to progress, roadblocks and most importantly the potential pitfalls that may be holding the industry back from establishing clinical application breakthroughs. This document further highlights some significance of the most 'dependent projections' of the cornerstones from which the art of stem cell engineering evolved while advocating the progression of the art with an added level of meticulous re-evaluation and emphasis on metabolic state, state of extracellular environment (ie. internal environment) and age of donor cells recruited in the technology.

Finally, it becomes very rewarding when researchers' output meet at a juncture where nature tangents and aligns with the stem cell scientific breakthroughs. Therefore, our scientific and clinical goals are morally encouraged in this direction as it is only then that we can appreciate the current challenges faced with incurable diseases and ailments that plague humanity bundled with metabolic and senile-related entities while attempting to enhance longevity and the quality of life in patients and the general population.

Revering Bio-Developmental Concepts in Address of Stem Cell Manipulations

A window view of the stem cell research spectrum precipitates promise of hope as well as unprecedented fears following stem cell manipulations. These opinions have not deterred scientists from further expansions and investigations into the subject matter. Rather, ideologies stemming from positive steps have evolutionized into and encouraged more safer methodologies of art, leading to further development of this solidifying facet of research focus. In the past years, Embryonic Stem Cells (ESCs) manipulations have projected an alarming confetti of global and ethical controversies surrounding their harvest, cultivation and the contingency of genetic aberration and inclinations that may potentially cause harmful effects to health and life. Today, an offshore approach of the ESC lines is the Somatic Cell Nuclear Transfer (SCNT) technology albeit this newer ESC lines method is also fraught with a kit of limitations regarding its efficiency in application and also, has not satisfactorily relayed the anticipated benefits for its recruitment purpose(s).

It is therefore pertinent that all scientists in the field who are not abreast with the basis of developmental biology, if need be, revisit their knowledge background and deeply understand the concepts and phenomena of totipotency, pluripotency, multipotency, oligo potency and unipotency as well as germ-line transitional patterns as it appears that a much deeper comprehension of these armaments is what holds the 'bundled keys' potentially fit for unlocking the residual overpowering stem cell abysses in the currently attempted emulation efforts of stem cells for the exposure of their apodictic behavioral patterns for their application purposes.

The Pros and Cons of the Stem Cell State of Art

It can be rewarding when well understood that one of the prime goals of stem cell studies and current efforts are aimed at enhancing the quality of life, if possible, prolonging it through anticipated regenerative medical applications. This is a worthwhile journey embarked on, with the hope of unlocking the versatility of genes through scientific knowledge and application efforts. This same art of stem cell engineering also holds significant and promising breakthroughs that when combined resources (including; human, financial and scientific) at all levels are properly rendered and allocated, the fine lines that may complete the art-piece as from our current standpoint and view may become credible and potentially applicable in a condensed amount of time. It currently appears that

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scientists and experts in the field are still facing major roadblocks leaving them at a milestone that can only be appreciated at the experimental (animal model) frame.

Some of these challenges encountered at this experimental phase are residuals delaying or preventing clinical applications through trials and treatments of human subjects in need. It is concerning and sometimes overwhelming when consideration is given to the amount of revenue(s) invested in support of stem cell exploratory efforts and yet, are still foiled by nature's secret embedded in this characteristic area. This current juncture in the observed scientific progress regarding stem cells engineering highlights the unique importance of the integral omnipotence of our 'internal environmental playing powers' that despite decryption of certain essential *in vivo* factors that favor stem cells manipulation to a certain degree, scientists are still provocatively baffled and lambasted by the inherent synergistic forces or factors that ensure stem cells' favorable, replicating and stable states dictating our outcomes of health, disease, survival or wasting away.

Induction versus Somatic Cell Nuclear Transfer in Clinical Applications & Trials

The induction of somatic cells into pluripotent stem cells by introducing induction factors has rapidly become pervasive, overriding and replacing some known earlier orthodox experimental methodologies in the field in just a dozen years. These manipulated cells employed in this approach become Induced Pluripotent Stem Cells (IPSCs). But, are we there yet? -- a point where we can implement this induction approach outcomes in large scale clinical trials and treatments? It's hard to render an an unequivocal response to that open-ended question.

Interestingly, Somatic Cell Nuclear Transfer (SCNT), a current standard has modernized and civilized the ESC approach but still operates at a low efficiency. Current conundrums and controversies surrounding ESC lines are the issues of single blastomer cell derivation, Cdx2-inactivation and contingent pathogenesis and together, all these issues particularly develop a hurdle for potential clinical applications and further breakthroughs.

Some Adult Stem Cell (ASC) lines have been engaged in the treatment of human subjects or participants, however, majority of ESCs and IPSCs still remain at the experimental level and mostly in animal subjects. Progress has been seen in animal model experiments with the utility of IPSCs for sickle cell anemia and Parkinsonism treatments, the results of which can be appreciated in subject outcomes after IPSCs treatment with improvement, restoration of cardiac function following injection of ESCs as well as improvements in symptomatic stroke with ESCs derived neurons. With the awareness that, outcomes of certain stem cells have not yet qualified for translational applications is a clear reflection of the finishing standoff owing to the limitations of the engineering art as well as their potentially hopeful but far-fetched anticipated future applications in human subjects anytime soon.

Age-Factor and Metabolic-Internal Environment as Potential Induction Apparels

As stem cell technology primarily aims at closing in on uncovering the underlying ocean-floor of the potential cause(s) of age induced degeneration while advocating for age-spectra regenerative capabilities, it is important to also hammer on the 'potential life remaining span' of the utilized donor cells and their corresponding factors and genes that are manipulated. Logically, it can be accepted that the engagements of these inductions and nuclear transfers do require specific substrate media or micro-environmental state to enhance achievement of manipulative goals, as exemplified in nuclear transfer approaches where enucleated cells are starved. It can be understood that these starved cells consequently yearn to thrive in the donor substrates, a phenomenon that keenly highlights the importance of the essence quality within the micro-environment of the substrate required to establish success rates of the SCs biochemical processes involved in the engineering art. The other side of the coin being that, from a physiological standpoint, it can be viewed that absolutely nothing can replace the eminent constitution of our individualized inherent extracellular environment endowments, that is to say; 'specific internal environment status' which is undoubtedly impregnated with the essential factor essences necessary for successful tailored inductions that target specific *in vivo* genetic responses *via* their expressions in specific individuals. The excerpts from these notions candidly indicate a perpetuated metabolic or nutritional attire at display which further lay emphases on advocating critical evaluation of donors' age, pre-existing health condition(s), immune as well as metabolic and nutritional states during selection of donors for stem cell engineering purposes.

How Far Down are we from the Tip of that Ice-Berg?

As scientists learn to sway away from techniques considered unethical that subsequently spark outrage and dilemmas, it is also important to note that within a condensed amount of time since the year 2006, after the well renowned scientists in this engineering masterpiece; Takahashi and Tamanaka introduced their induction cocktail factors for induction utilization of PSCs, paramount number of research efforts that evangelize their methodologies have emerged, all of which clear the path of the previously perceived hypothesis in the field and setting a compass for a potentially formidable top-notch regenerative breakthroughs in the near future. Considering the likelihood of capabilities of some of these inductions studies, they surely do encourage well-benched scientists to reconsider and explore further in their quests for a promising outcomes. Some of these promising advancements can be exemplified in scientists efforts to recruit human based circulating blood macrophages and reprogram these cells into pluripotent stem cells while using engineering approaches that engage these peripheral blood cells through specific media passages for the seedlings to behave like cartilage cells through their expressions of specific chondrogenic lineage of clusters of differentiation (CD73&CD105) of the mesenchymal stem cell origin. This unique finding together with many other rewarding studies by scientists in the field portray an immense picture of our closeness to narrowing the limiting gaps that measure our current difficulties in the field between now and the near future.

What the Future May Hold on Stem Cell Ergonomics

The future is close but yet far when scientists and field experts

consider our current roadblocks encountered on our mundane engineering research efforts to establish regenerative pathways and reliable breakthroughs. Efforts are morally encouraged to continue but with deep caution.

With the availability of current technological advancements and resources that include three-dimensional-technology, nano-technology, artifical intelligence, it would be morally encouraging to apply employ these resources to guide our scientific and clinical goals towards patient-specific applications of stem cell therapy in a well-tailored and safest approach.

Finally, it is strongly recommended that propagated engineering efforts aim at inviting most minimal errors, efficiency, safety as well as cost-effective measures for a potentially successful and sustainable acknowledgment in the anticipated future.

Aurthor's Contributions

NVH-L designed and drafted the letter. CMB contributed to vital information on material content and TL and YLX revised and gave the final approval of this letter. All authors read and approved the final letter-manuscript.

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