Impact of deploying a Genetic approach to Stem Cells opens-up new facets in the "Blank Slates" of our body

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Abstract: Since the dawn of the Post-Genomic era (25 years back), applying a genetic approach to solving various intricate problems/issues in research has taken-off even more swiftly than ever before. Spatio-temporal cues defined for certain critical components in a particular developmental pathway (involved in causing/progression of certain disease) provide a firm basis for detecting the order, hierarchy and "switching-off or on" of genes that regulate it. The various time-points, at which genes are switched on/off, clearly determines the fate of what a cell does in terms of being functional or non-functional, due to disruption of that specific pathway. Recent research-work in this area provides strong evidence, toward identifying such components (associated with Wnt-signaling involved in Colorectal Cancer-CRC disease). These crucial elements indeed determined the genetic transformation of a "blank slate" ("cells of origin" and/or putative "cancer stem cells") or "primitive-state" epithelial cells to an intermediate adenoma/polyp (dyspastic), and later to a proliferative (hyperplastic) or cancerous (neoplastic) state. The idea is to re-iterate the power of genetics, in solving and filling the missing links of any developmental pathway involved in progression of a disease (in this case, CRC). A critical temporal requirement of certain molecules [Caesin-Kinase I (CKI) and Human-Discs large (hDlg)] was finally established and these proteins were identified as "early" and "late" acting molecules respectively, in a very crucial developmental event, that basically transforms "polyps" to full-fledged "carcinomas" (epithelial cancers) in COLORECTAL tumors. The detection of these genetic and developmental parameters, served as a focal-point and a prominent diagnostic feature, for detection of effects, i.e., Gain/ loss of other components involved during progression of CRC disease. Coincidentally, the chromosomes on which these genes reside have been found to be dense and rich in SNPs (hot-spots), the details of which were published in a separate report (Patidar & Bhojwani, 2013). This work harnessed the potential of Genetics, Developmental Biology and Bio-Informatics tools to solve a long-standing puzzle in pin-pointing some genetic factors that were critically involved in the progression of CRC disease. The report has created enough impact, in terms of authentically suggesting, that it is only when we deploy a combinatorial approach towards certain complicated biological problems, can we successfully unveil the underlying mechanisms in greater details. However, it is now conceived that, at the heart of every tumor lies a rare sub-population of cells (Cancer Stem Cells-CSCs), which give rise to most of the Cancers and are now the targets of investigation. Since no definitive markers or efficient labeling tools are available, this population of cells still remains elusive in both cancer and stem cell biology. Therefore, it would be critical to understand molecular differences between stem cells and cancer cells, which might be helpful in providing novel insights into the mechanism of tumorigenesis as well as potential therapeutic targets, in foreseeable future. We have come a long way in the stem cell advances over time. Very recent breakthroughs include: (a) The tuning and genetic re-programming of stem cells (iPS cells) by a handful of genetic factors. The transformation of cancerous cells to normal cells by reversing the genetic changes involved and also restricting the awry cancerous cells by using microRNAs (http://yournewswire.com/ breakthrough-scientists-find-way-to-change-cancer-cells- into-healthy-cells/).

Introduction: Hereditary breast cancer has some interesting biological differences compared with apparently sporadic cancer. In breast malignancies from patients with a BRCA1 mutation, a greater proportion are high grade and histologically medullary or atypical medullary in type.

Therefore, in individuals with bilateral medullary/atypical medullary cancer, the probability of BRCA1 mutation should be very high. This will need to be confirmed by further studies. At the present time, no other histopathological type is associated with mutations in particular susceptibility genes. Nonetheless, finding bilateral breast cancers or multiple primary tumours will increase the chance of hereditary disease.

Both lobular carcinoma in situ (LCIS) and atypical hyperplasia have been associated with family histories of breast cancer. The 10 year risk of invasive disease in association with family history is approximately 40%. Skolnick et al suggested that persons with LCIS were more likely to have a mother or sister with breast disease than with other tumour types. The Breast Cancer Linkage Consortium, however, demonstrated that LCIS was less common in carriers of BRCA1 and BRCA2 mutations than in sporadic control individuals, although this did not reach formal statistical significance. Skolnick et al [16] did not find a significant statistical association between ductal carcinoma in situ (DCIS) and family history. This was supported by the Breast Cancer Linkage Consortium data, which found fewer cases of DCIS among BRCA1 mutation carriers than among control individuals. The rate of DCIS in BRCA2 mutation carriers was similar to that in sporadic control individuals, however. It may be that proliferative breast disease is a marker for BRCA3/BRCA4. The evidence from histological studies for the association of specific types of tumour with BRCA1 and BRCA2 mutations will allow a directed approach to genetic testing of breast cancer families.

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