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Cycles of Micro-Environmental Re-Modulation as induced Gliomagenesis and Tumor Progression

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Abstract

Dimensions of re-constitution are integral events of renewal of a putative tumor stem cell that subsequently re-tabulates processes of renewal as evidenced by identity switches that perform angiogenic and proliferative processes of integration. The infiltrative attributes of a glioblastoma permit a realization of global permissiveness that promotes plastic dimensions of attempted re-constitution in a region of re-modulated micro-environmental re-conditioning as further proposed and sustained by an expanding lesion of proliferative capability and of suppressed apoptosis.

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Introduction

The concept of dynamics of glioblastoma can be reviewed in terms of Newtonian forces as regards particularly to the inherent infiltrative phenotypic attributes of high-grade gliomas. The conglomerate clustering of such neoplasms in terms strictly of biologic progression is reflected in the histo-pathologic and clinical dimensions of a glioblastoma; this is therapeutically resistant to current therapeutic measures, both in terms of inhibition and elimination of the lesion in the individual patient.

Distributional reactive phenomena are inclusive dimensions of infiltrative behavior as attested by angiogenesis in particular. Specific roles for Vascular Endothelial Growth Factor (VEGF) and its induced permeability and vascular leakage in Gliomagenesis have remained unclear; VEGF, however induces tumor edema and tumor spread [1]. The performance attributes of glioblastoma is further reinstated at every stage in the unfolding of molecular events in p53, RAS, PI3K, RB and in growth factor receptors such as platelet-derived growth factor receptor.

Epidermal growth factor like domain 7 regulates glioma angiogenesis, and silencing of this gene, and cell adhesion is inhibited with failure to develop a lumen morphology of the vessels [2].

Receptor stimulation

Dimensions of incoherent or incongruous stimulation cues attest for a disorder in concomitant events and are determinants in the modulation of remodeling of extra-cellular matrix within which the infiltrating glioblastoma evolves. Expression of endothelial and mesenchymal markers (ANGPT2, CHI3L1) showed a stronger contribution to the micro-environment to the emergence of the mesenchymal subtype than the tumor biology itself [3]. The fully constitutional profile of forces determining infiltration of the stromal micro-environment indeed testify to a turnover disequilibrium that transcends the cycling proliferative activity and loss of apoptosis.

Real indices of progression relate to the volume of tumor tissue that correlates in terms of the infiltrative profiles of glioblastoma. Alternating index dynamics are primarily an infiltration that in turn strictly modulate in dominant fashion the determinants of enhanced growth dimensions. In a substantial process of modulatory reshaping of the micro-environment, there emerges an infiltrative phenomenon that primarily characterizes the pathologic and clinical properties of glioblastomas.

Tumor biology

Tumor biology can be translated in terms of a dynamic disturbance in equilibrating forces of action and reaction, beyond the shaping and re-shaping profiles of an infiltrating front of the glioblastoma. The various, numerous indices of pathobiologic activity are inherently related to the tumor malignant transformational process that in turn is assessable in terms of the infiltrative tumor behavior. Targeting and reducing glucose uptake with small-interfering RNA-based nanomedicine bulks glioma cells in a glucose restricted tumor microenvironment and reduces GLUT3 (glucose transporter 3) in glioma cells [4].

Transcriptional factors and receptor stimulation are phenomenal autocrine and paracrine dimensions of modes of interference that inferentially modulate both the glioblastoma lesion and the micro-environment. Effective block of the migratory ability of cancer cells by inhibiting protein kinases and subsequent induced cytotoxic stress may be instrumental in therapeutic outcome [5]. The profile specificities deterministically re-modulate dimensions of resistance to therapy and induce a recurrence of the neoplasm.

Biophysical reactivation is the core phenomenon constituting the invasive phenotype of glioblastomas in a manner that constitutively and inherently modulates the neoplasm and presents novel attributes of replacement of the microenvironment and of its specific constitution. Brain microenvironment critically influences methylation and transcriptional patterns of glioma stem cells [6].

Malignant Transformation

The determination of a malignant transformation process is the true attribute of the process creation of an invasive phenotype that resists re-modulation and reversal to normal equilibrating dimensions. The performance of biologic tumor emergence is attested by the profile accumulation of genetic lesions that delete or mutate the suppressor tumor genes and activate the oncogenes. It is such accumulative phenomenon that profiles such tumor emergence in terms of further promotional dynamics of infiltrative tumor behavior.

A replacement constitution therefore combines tumor infiltrative front delineation with the processes of angiogenesis and suppressed apoptosis. In real terms, the further progression of the lesion is fabricated and re-modeled in terms of micro-environmental conditioning. The performance dimensions can be equated to the propositional concept of disequilibrium that allows permissive constitutional reinforcement of Newtonian biophysical forces of action and reaction, as reflected especially in micro-environmental re-modulating cycles of replacement and attempted repair.

Hypothesis of re-modulation

A hypothesis concerns the constitutional malignant re-emergence that is therefore cyclical in the forward motivations of induced receptor stimulation and in terms that further contribute to constitutional self-evolution. The embryonic developmental processes do constitute the performance attribute dimensions that inherently call into operative dimension the HOX genes in particular.

Macrophage colony stimulating factor modulates growth, proliferation and differentiation of hematopoietic cell lineages; it is secreted at high levels with recruitment of macrophages to the tumor microenvironment [7].

Distributional phenomena of incongruent parallels of evolving tumorigenesis characterizes further the angiogenesis that transcends the constitutional and further pathologic modulation of the micro-environment surrounding and constituting part of the neoplastic process of growth and replacement of the micro-environment in the infiltrative zones of the glioblastoma. Diffuse infiltrative gliomas blend extensively in the brain micro-environment [8].

A real dimensional spread of malignant cells comes to operatively re-distribute the characteristic properties of a neoplasm that primarily infiltrates and only secondarily grows and expands its constitutional components.

Re-Distributional Forces

Re-distribution of malignant attributes of a glioblastoma lesion is attested phenomenon to the replacement of micro-environmental pre-conditioning in a manner; this specifically continues as amplified forces of attempted reconstitution of tissues and by repeated reconstitution of the tumor lesion and of its evolutionary attributes of malignancy. The recruitment and activation of regulator T cells in the brain glioma microenvironment induces detrimental reduction in antitumor immune responses [9].

Performance attributes attest to a relative series of events that involve volume of the glioblastoma to the involved parameters of infiltrated tissue, on the one hand, and of area dimensions of necrosis within the tumor itself. In such manner, the neoplastic progression is a performance index of relative replacement of the micro-environment that progresses as evolutionary tumor constitution.

The interactions of abnormal cell migratory mechanisms and of the glioma microenvironment likely differentiate cancer from normal cells [10].

Re-appraisal phenomena of component participation in Gliomagenesis are reflected in the concept of stem cell biology that repopulates and further re-dimensionalizes such evolution within the terms of development characterization and re-characterization of malignancy phenomena.

Lesional Realization

Realization of infiltrative fronts is therefore a congruous determination within a scope phenomenon of replacement as further evidenced by the expansion of tumor cell growth and of neoplastic re-distribution of malignant attributes. The angiogenesis is further constitutionally determined within parametric fields of evolution as determined by developmental forces of genesis with thus replacement of the micro-environment. Mouse models provide insights into the influence of the tumor micro-environment and of mutations within contexts of transformation [11].

Self-promotional change is directional in its determined scope for further adaptation beyond the simple process of constitutional replacement and thus attests to tumor biology beyond forces of distribution and replacement. As such, the further re-characterization of dimensional spread is a function parameter of disequilibrium that comes to progress as micro-environmental re-conditioning and as simple amplification processes in their own right.

Glioma cells and neural stem cells may interact at the niche or micro-environmental levels to induce proliferation and differentiation of neural stem cells and to suppress proliferating glioma cells [12].

Amplifying determinants are significant parameters in the genetic lesion creation that involves the performance dimensions of malignancy phenomena per se. Fluorescence microscopy can provide high spatial, spectral and temporal resolution and together with

the use of 3D microscopy based on confocal, structured or single plane illumination may allow the study of interactions with the micro-environment [14].

Concluding Remarks

The biologic significance of performance determination is an integral process of promotional replacement phenomenon that contributes to the identity of a progressive infiltrative process that resists current modes of therapy in glioblastoma patients [14]. Glioma-infiltrating microglia are capable of innate immune responses including phagocytosis, cytotoxicity and Toll-like receptor expression [15].

The further promotional re-distribution of biologic events evidences the relative and mechanical dimensions of performance that involve the disequilibrium of change and replacement in terms strictly of lesion constitution and of micro-environmental conditioning and re-conditioning. A high matrix metalloproteinase/and TIMP-2 (a specific tissue inhibitor) may account for absence of extracellular fibronectin and allow the participation of tumor cells in the proteolytic degradation of the extracellular matrix [16,17]. Imbalance of elevated levels of plasminogen activators and of plasminogen activator inhibitor-1 in the tumor micro-environment is implicated in glioma cell invasion [18]. Oncogenic Ras appears a significant contributor to tumor cell invasion and angiogenesis, within the added context of the tumor's microenvironment [19]. Normal brain tissue is capable of producing laminin, collagen type IV and fibronectin when infiltrated by glioma cells [20]. On the other hand, glioma cells are able to adapt their cytoskeleton to their micro-environment by producing glial fibrillary acidic protein [21]. It is in view of the overall integrity of glioblastoma lesions that the micro-environment is re-constituted as further performing attributes of a stem cell biology that self-renews and differentiates as subsequent dimensions of progressive de-differentiation.

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