

EC CLINICAL AND MEDICAL CASE REPORTS Guest Editorial

Toll-Like Receptors-Autophagy Immuno-Inflammatory "Molecular Intersections" in Tumor Microenvironment in Complex Gastro-Hepatic Diseases Primarily Colorectal Carcinoma: Translational Research Impact in Genetically Susceptible Populations in Covid-19/Omicron Pandemic Era

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Dissecting the underlying cellular, molecular and genetic basis of inflammatory hypoxic tumor microenvironment in complex gastro-hepatic diseases especially colorectal carcinoma warrants dynamic timeline-driven evidence-based global collaborations in clinical research with eventual design of immuno-therapeutically safe patient-friendly cost-effective treatment modalities in the distressing Covid-19/Omicron pandemic era. A sophisticated "genetic blueprint" with emphasis on early risk-assessment, risk-stratification, diagnosis and immune-metabolic genetic subgrouping of early vs advanced tumor stage and grade of colorectal carcinoma is warranted for cost-effective gastro-hepatic disease management amongst genetically susceptible cohorts worldwide. The disproportionate share of morbidity and mortality amongst genetically and ethnically heterogeneous population-pools symptomatic of early vs advanced stage/grade colorectal tumors is certainly intriguing; public health-oriented clinical management endeavors for meaningful patient-centric evidence-based pragmatic outcomes for successful design and development of clinically validated biomarkers for colorectal management would prove to be a "gastro-hepatic carcinogenesis genetic roadmap" for patient-friendly immunotherapeutically safe precision medicine-oriented treatment.

In my expert opinion, enthusiastic clinical researchers worldwide should strategically and dynamically collaborate and actively investigate the complex gastro-hepatic-immune signaling "molecular genetics-metabolic-oncogenomics cross-talks" in colorectal carcinogenesis by selective immunotherapeutic targeting of biochemical/metabolic signaling networks viz. Toll-like Receptors-Autophagy-Apoptosis-

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Ceramide/Sphingolipids-Wnt/Frizzled, etc. in aberrant physiologic mileu in the inflammatory gastro-hepatic tumor microenvironment with vascular insufficiency along with hypoxia, coupled with precision-based transcriptomics, proteomics and metabolomics for eventual design of cost-effective predictive and/or prognostic biomarkers, novel drugs and pharmacological scaffolds for personalized "tailor-made gene therapy" in genetically susceptible population-subsets of asymptomatic vs borderline and symptomatic cohorts of varying ethnicities/life-styles in the unpredictable Covid-19/Omicron pandemic era.

Furthermore, cross-sectional/longitudinal/prospective/retrospective innovative study-designs with logical inclusion and exclusion criteria along with adherence to core tenets of good clinical practice, scientific integrity and bioethics, enrolling adequate samples of clinically confirmed cases of colorectal carcinoma and age-/ethnicity-matched healthy disease-free controls from random population(s) with a case-control genetic association epidemiology pharmacogenetics/genomics approach would prove immensely beneficial in risk-stratification of early vs advanced grade/stage of inflammatory colorectal carcinoma of heterogeneous tumor core(s) with distinct cell-types; considerable statistical power with an adequate sample-size leading to minimal selection-bias warrants collaborative multicentric gene-epidemiology studies conducted by biomedical researchers to draw meaningful conclusive interpretation of the data-sets thereby yielding unambiguous reproducible end-points for evidence based clinical management of colorectal carcinoma along with other gastrohepatic disorders/ailments of complex etiopathogenesis.

Eventually, evidence-based pragmatic colorectal carcinogenesis-immunomodulation-based innovative therapeutics and oncogenomics in timely clinical management of disease-susceptible cohorts of ethnically disparate populations worldwide warrants precision-oncology intervention(s). The biochemical/metabolic cross-talks amongst the enigmatic array of TLRs and Autophagy signalosome primarily Beclin-1, Microtubule-associated-Light-Chain-Protein (LC-3) isoforms I and II, Atg 2/5/7 and apoptosis/necrosis markers Bcl-2 and High-Mobility-Group Box-1 (HMGB1), and Ceramide/Sphingolipid-Wnt/Frizzled signaling cascade are emerging as elegant "immune molecular rheostats" for development of predictive and/or prognostic biomarkers and pharmacological scaffolds in timeline-driven cost-effective risk-stratification and management of colorectal carcinoma in ethnically susceptible populations worldwide in the Covid-19/Omicron pandemic era [1-3].

Financial Disclosures

The author has no relevant financial disclosures and/or conflicts of interest to declare.

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