

## Autophagy-Toll Like Receptors-Wnt Biochemical Signaling Cross-Talks in Trafficking of Coronovirus Viral "Spike" Proteins: Immunotherapeutic Potential for Biomarker Development in Prostate Cancer, Cervical Cancer, Colorectal Carcinoma and Glioblastoma in the Covid-19 Vaccine Era?

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Dynamic innovative clinical research collaborations spanning genetically disparate population-subsets of diverse ethnicities are urgently warranted to identify novel cellular/molecular/genetic molecular regulatory networks/cross-talks in the inflammatory Coronavirus-microbiota associated complex viral protein-trafficking for developing innovative Toll-like receptors (TLR)-Autophagy-Wnt "immunogenic cell death"-based pharmacological scaffolds/biomarkers for risk-stratification of inflammatory cancers primarily Prostate Cancer, Cervical Cancer, Colorectal Carcinoma and Glioblastoma in the Covid-19 vaccine era.

In this context with emphasis on evidence-based good practice clinical research adhering to core tenets of bioethics that I gained at Graduate Schools of Biomedical Sciences and Schools of Medicine at prestigious Universities/Medical Centers in States of Texas, Nebraska and New York, USA, I hypothesize that precision-based predictive risk-assessment model amalgamating Covid-19 vaccine-related risk-assessment global trends in ethnically disparate asymptomatic vs symptomatic population-subsets of both high vs low-resource settings is essential for significantly reducing the disproportionate share of morbidity and mortality associated with latent and fulminant Covid-19 positivity in symptomatic prostate, cervical and colorectal carcinoma subsets of cohorts of varying genetic landscapes in susceptible populations worldwide; synthesis of pilot data-sets on Autophagy-TLRs-Wnt in trafficking of Damage Associated Molecular Patterns/Viral envelope proteins including complex array of cell-signaling networks in nucleocytoplasmic shuttling/lysosomal degradation in aberrant inflammatory metabolic/physiological milieu for developing a hypothetical public health Covid-19 vaccine-related patient-friendly prostate cancer research model for clinical development of predictive biomarkers in Covid-19 vaccinated multi-centric cohorts asymptomatic or symptomatic of Covid-19 and/or Omicron infection (RT-PCR/Rapid Antigen test Covid-19 positivity) with clinical manifestation of benign prostate hyperplasia and prostate cancer pre-/post-robotic prostatectomy, Human Papillomavirus-mediated cervical cancer, metastatic colorectal carcinoma and glioblastoma.

**Public health impact:** "Immunogenic Cell Death" signaling networks regulated by "TLR-Autophagy-Wnt" biochemical/metabolic interactions have significant immunotherapeutic potential for innovative pharmacological scaffolds and predictive/prognostic biomarker development in North American, European (British, Danish, Nordic, etc.) and Asian Indian (North Indian vs South Indian) Coronavirussymptomatic patients of genetically distinct landscapes and socioeconomic-strata pre-/post-vaccination (Covishield or Covaxin Dose(s) 1, 2 and 3/precautionary) manifesting with early vs advanced prostate cancer with diminished fertility potential/erectile dysfunction pre-/post-robotic prostatectomy, HPV-positive cervical cancer (FIGO stages 1 vs II vs III vs IV), colorectal carcinoma and glioblastoma. Viral protein-trafficking and endocytosis of "spike" proteins involves a complex interplay of Autophagy-TLRs-Wnt immune-inflammatory signaling networks thereby warranting future translational and clinically impactful research in this nascent Covid-19 vaccines' era in susceptible cohorts of prostate cancer, cervical cancer and colorectal carcinoma in New York, Texas, Nebraska and adjoining states of United States of America and "at-risk" ethnically disparate populations worldwide. In my expert opinion, immunogenic cell death-mediated biochemical/metabolic intersections in the inflammatory tumor microenvironment offer fascinating avenues for future cancer-stem cells'

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patient-centric public health oriented meaningful research and eventual precision-based innovative molecular oncology-related immunotherapeutics in cost-effective management of an array of carcinomas: prostate/cervical/colorectal and glioblastoma.

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02