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Unresolved inflammation and aging: Joined forces in the induction of chronic diseases and cancer

Claimed cancer 'personalized' medicine' or 'targeted' therapies which are based on the use of inhibitors of molecular components (e.g., gene mutations, growth factors, kinases) that identified in site-specific cancers demonstrated high rates of failure (85-95%) in the last few decades. The design of costly clinical trials and drugs that use potent apoptotic factors clearly indicate: a) poor, fragmented and fuzzy understanding of cancer biology that are costly to the cancer-stricken public; b) majority of 'targeted' drugs produce serious and life-threatening side effects such as drug-resistance, cancer relapse, cachexia, anorexia, multiple organ failure and death, symptoms that are similar to potent pathogen-induced acute inflammatory diseases such as sepsis, meningitis, salmonella poisoning, major trauma; c) an effective immune system provided via acute inflammation routinely monitors and destroy cancerous cells and other harmful components; and d) cancer only become a threat to body when immune system loses its effectiveness, particularly during aging. To better understand the forgotten but fundamental role of immune surveillance, this presentation will focus on the loss of cancer surveillance and chronic inflammation in the induction of a wide range of age-associated diseases or cancer. The results of our 'accidental' discoveries in 1980's on experimental models of acute and chronic inflammatory diseases are suggestive of the first evidence for a direct association between inflammation and tumorigenesis and angiogenesis (Khatami et al 1984, 85, 88, 89, 91) and a first report on developmental phases of inflammation-induced immune dysfunction (Khatami 2005). These studies were extended at NCI/NIH since 1998 during design of clinical trials, utilization of patient biospecimen for cancer molecular diagnosis and prevention. Acute inflammation was defined as highly regulated cross talks, possessing 2 biologically opposing arms, 'Yin' (pro-inflammatory, apoptosis or tumoricidal) and 'Yang' (anti-inflammatory, wound healing or tumorigenic) between immune and non-immune systems (vasculature and neuro-endocrine). Chronic (oxidative stress, persistent or unresolved) inflammation was defined as loss of balance between 'Yin' and 'Yang' (tumoricidal v tumorigenic) of response profiles that could create immunological chaos in target tissues. Unresolved inflammation and severe alterations in immune dynamics, 'immune tsunami', could differentially impact tissues that are naturally immune-responsive (e.g., epithelia, endothelia, stroma, vasculature) or immune-privileged (e.g., blood brain barrier/BBB, CNS, cornea, neuroretina, reproductive system, hair follicles) by damaging architectural integrity of tissues and induction of acute (e.g., sepsis, meningitis, respiratory failure) and age-associated chronic diseases such as neurodegenerative and autoimmune diseases, diabetes and cardiovascular complications or cancer. Future directions in design of clinical trials will be proposed based on promotion of inherent ability of immune surveillance, or the maintenance of balance between 'Yin' and 'Yang' of acute inflammation. The ultimate goal is to help resolve the mystery around cancer biology and end the misery of cancer-stricken public.

Biography

Mahin Khatami received her Ph.D. in Molecular Biology from University of Pennsylvania (UPA, 1980), after receiving her MA in Biochemistry (SUNY, Buffalo, NY), BS and MS (Chemistry and Science Education, Iran). Her postdoctoral trainings were in physiology, protein chemistry and immunology at UPA, U VA and Fox Chase Cancer Inst. As a Research Faculty (Dept. Ophthalmology at UPA) she was involved in two major projects, diabetes complications and experimental models of acute and chronic inflammatory diseases. In the first decade of her research career at UPA, by publishing 39 scientific articles and 60 abstracts in conference proceedings, she became the most productive scientist in USA. In 1998, she joined NCI/NIH as a Program Director, involved in major clinical trials (PLCO). Her relentless efforts for promoting the important role of inflammation in cancer research paid off in the last few years as significant funded projects are currently devoted to various aspects of inflammation within and outside NCI/NIH. Her last position before retirement at Professor level was Program Director, Innovative Molecular Imaging Technologies, (IMAT) and Assistant Director, Technology Program Development, Office of Director, NCI/NIH. She is currently Associate Editor for Cell Biochem. Biophy, Editor and author of books on inflammatory diseases and cancer.

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