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Rebounding of dendritic cells post chemotherapy: Implication for cancer immunotherapy

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The success of anti-tumor immunity depends on the generation of functionally effective T cells. Adoptive cell therapy (ACT) of autologous tumor-reactive T cells after chemotherapy a nd followed by vaccination is a promising approach for generation of functional T cells for cancer immunotherapy. This ACT modality consists of in vitro stimulation of T cells from a host own peripheral blood or tumor and then infusing them back to the same host blood followed by vaccination regimen such as peptide or peptide-pulsed dendritic cells (DCs). The host is irradiated or treated with chemotherapeutic drug such as cyclophosphamide (CTX) prior ACT to induce lymphopenia. The cellular and molecular mechanisms underlying the beneficial effects of lymphodepletion in the context of adoptive T cell therapy and vaccination, however, are not well understood. Defining these mechanisms would significantly improve the application of lymphodepletion to ACT. Our recent studies have identified expansion of DCs, the central player of immune response, as a potential mechanism. We have utilized the toll-like receptor 3 (TLR3) agonist poly(I:C), a synthetic viral mimic double-stranded RNA, to induce the full activation of DCs expanded in vivo after chemotherapy and during vaccination with defined tumor antigens, resulting in efficacious therapeutic anti-tumor responses. Our results reveal that the combination of T cell therapy and vaccination in the presence of a potent adjuvant such as a TLR agonist at precise timing post chemotherapy opens a new avenue for cancer immunotherapy that can be translated into the clinical setting to cure different cancers.

Biography

Mohamed L. Salem is the Professor of Immunology at Tanta University, Egypt. He obtained his PhD in 1995 from Tanta University, Egypt and Kyushu University, Japan through a PhD scholarship from the Ministry of Higher Education, Egypt. From 1997 -2001, he was a Postdoctoral Fellow at Kyushu University, Japan and from 2002-2010 as an Assistant Professor at Medical University of South Carolina, USA. Dr Salem was awarded the State Incentive Award in 2004 and the State Excellent Award in 2010 in Basic Sciences from the Academy of Scientific Research and Technology, Egypt. He has published more than 60 articles in peer-reviewed journals and more than 60 national and international workshops and conferences in Immunology.