Zvi Granot, Madridge J Cancer Stud Res. 2016
http://dx.doi.org/10.18689/2640-5180.a1.002

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International
Cancer Study & Therapy Conference

April 4-6, 2016 Baltimore, USA

The ratio between distinct subsets dictates overall neutrophil contribution in cancer

Zvi Granot
Dept. of Developmental Biology and Cancer Research, Faculty of Medicine, Hebrew University, Israel

In recent years it has become apparent that the non-malignant stroma surrounding tumors plays a critical role in the processes of tumor initiation, growth and metastatic progression. In this context the part neutrophils play has been a matter of debate. Neutrophils are the most abundant leukocytes in the human circulation and are usually associated with inflammation and with fighting infections. In cancer, neutrophils were shown to provide a variety of pro-tumor functions including secretion of tumor promoting cytokines, degradation of the ECM, immune suppression and more. In contrast, neutrophils were also shown to have the capacity to kill disseminated tumor cells either through direct cytotoxicity or via antibody dependent cytotoxicity. These conflicting reports suggest that although neutrophils are largely viewed as a homogeneous population they may consist of distinct subsets with significantly different properties. Indeed, we identified a heterogeneous subset of low-density neutrophils (LDN) that appears transiently in self-resolving inflammation but accumulates continuously with cancer progression. While high-density neutrophils (HDN) maintain a pro-inflammatory, anti-tumor phenotype, LDN present with a reduced inflammatory profile, impaired neutrophil function and acquire immunosuppressive properties. In early tumor development HDN are the predominant neutrophil subpopulation giving neutrophils, in general, an anti-tumor phenotype. However, with tumor progression, LDN are preferentially propagated to the extent that they become the dominant circulating neutrophil subpopulation. When this happens the overall neutrophil contribution switches from anti- to pro-tumor. Our observations identify dynamic changes in neutrophil subpopulations and provide a mechanistic explanation to mitigate the controversy surrounding neutrophil function in cancer.

Biography:

Dr. Granot did his B.Sc, M.Sc and PhD at the Hebrew University in Jerusalem. His PhD thesis (2000-2005) dealt with the degradation pattern of StAR, a unique protein that is involved with steroid hormone synthesis. He then did a postdoctoral fellowship at the Hebrew University (2005-2007) where he focused on organ size control using pancreatic beta-cells as a model. Next, he did a postdoctoral fellowship at Memorial Sloan-Kettering, New-York, NY, USA (2007-2012). During this fellowship Dr. Granot focused on neutrophils, a subset of white blood cells that has the capacity to limit the metastatic spread. The understanding of this new role for neutrophils is very limited and requires further studies. Currently Dr. Granot is a PI at the Hebrew University in Israel, where he studies neutrophil versatility in cancer and the mechanisms that mediate tumor cell recognition and elimination by neutrophils.