**Rolling the Cancer Immunity Cycle**

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Immunotherapy is revolutionizing the treatment of cancer. The current immunotherapeutics that work by taking the brakes off T cells have been particularly transformational, dramatically improving outcomes for some cancer patients. But we still need to answer to those patients whose cancers do not respond to these immunotherapeutics, and those whose cancers respond initially but then become resistant to the treatments. The more we study the major issues of tumors, the more we come to realize that they cannot be understood in isolation. Tumors are systemic problems, which mean that they are interconnected and interdependent. Cancer cells are present within a complex adaptive ecosystem consisted of associated cells including immune cells, connective tissue cells, endothelial cells within a scaffold of matrix altogether forming tumor microenvironment. Cancer, perhaps uniquely among human illnesses, is a disease that arises through Darwinian interactions of microenvironmental selection and phenotypic adaptation, which are both causes and consequences of its complexity and heterogeneity. Since a life has begun 3.5 billion years ago, they ensured continuous interaction between the diverse species, both cooperative and fiercely competitive in nature. So they have developed complex and sophisticated immune system to survive. Can we develop better systems to fight against cancer than our own immune system? Even though we do not understand completely our own immune systems, we could try at least to awaken our own immune system to fight against cancer. In an attempt to trigger our own immunity against cancers, we utilized the characteristic of genetic instability to our advantage, as the expression of cancer cell neoantigens triggers immunity against cancer cells, which can be called “intrinsic cancer vaccination”. For patients who have nonimmunogenic tumors, we need to transplant xenogenic molecules to roll the cancer immunity cycle. For this purpose, we designed protein nanocages or extracellular vesicles (exosomes), which hold not only ligands or xenogenic molecules for enhancing cancer cell phagocytosis but also drugs for inducing immunogenic cancer cell death. This strategy will allow us to avoid using known tumor specific antigens, ex vivo manipulation and adoptive cell therapy, instead, efficiently present neoantigens of cancer cells to our immune system. This strategy could be combined with other treatment modalities to potentiate the therapeutic efficacy.