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CS1 (CD319) is an effective immunotherapeutic target for multiple myeloma

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Multiple Myeloma (MM) is a cancer of the plasma cells and is fatal without treatment due to anemia, renal failure, hypercalcemia, and bone destruction. Natural killer (NK) cells, a component of the innate immune system, function against infection and cancer. Identification and characterization of NK cell receptors lead to a better understanding of the molecular basis of Natural Killer cell recognition and activation by cancer cells. NK cell functions are regulated by a delicate balance between signaling through activating receptors and inhibitory receptors. We have identified and characterized CS1 (CD319, SLAMF7, CRACC) as an NK cell receptor activating its function through homophilic interactions. A monoclonal antibody against CS1 induced both Natural cytotoxicity and ADCC (Antibody-dependent cell-mediated cytotoxicity) by NK cells. CS1 is overexpressed on MM cells and anti-CS1 mAb enhance the killing of MM by NK cells. Elotuzamab (Empliciti) is a humanized monoclonal antibody against CS1, and has been aproved as a breakthrough drug against MM. During clinical trails, Empliciti in combination with chemotherapeutic drugs showed more effective than antibody treatment alone. However, the underlying mechanism for this is not known. We hypothesize that chemotherapeutic drugs induce the expression of CS1 on MM cells making them more susceptible to NK mediated killing. To investigate this property, MM cells were incubated with various combinations of chemotherapy and immunotherapy drugs in order to observe any change in surface expression of CS1. Our results indicate that treatment with anti-CS1 in combination with lenalidomide or doxorubicin and dexamethasone increased the cell surface expression of CS1. Thus enhancing the expression of molecular targets for NK cells is an effective strategy for immunotherapy of cancer.

Biography

Porunelloor A Mathew completed his PhD from University of Pune, India and postdoctoral studies at University of Medicine and Dentistry of New Jersey and UT Southwestern Medical Center, Dallas. Dr. Mathew, Associate Professor at UNT Health Science Center, Fort Worth, is a world-renowned Cancer Immunologist who identified and cloned human NK cell receptors, 2B4 (CD244), CS1 (CD319) and LLT1. Research in his laboratory showed that anti-CS1 antibody activates NK cell cytotoxicity against various cancer cells. Research in Dr. Mathew's group has lead to the development of novel NK cell based immunotherapy for cancer. He has published over 60 papers in reputed journals and serving as an editorial board member of repute.

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