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Tumor-derived CD200 inhibits the development of an anti-tumor response: Implications for immunotherapy

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Despite the extensive use of tumor-derived vaccines for treatment of CNS tumors, the suppressive tumor-bound protein CD200 has been overlooked to date. CD200 is highly expressed in a variety of human tumors. Our preliminary studies detected CD200 on multiple CNS tumors. This introduces a major problem for the development of tumor-based cancer vaccines. We are "shooting ourselves in the foot" by vaccinating patients with cancer vaccines designed to mount an anti-tumor response. CD200 acts as a checkpoint blockade when engaging its receptor CD200R. CD200 up-regulates peptidyl-prolyl isomerase A (PPIA), resulting in immune suppression. CD200 is expressed on endothelial cells within CNS tumor vessels down-regulating T-cell activation. We have developed a competitive inhibitor peptide overcoming CD200-induced immunosuppression. CD200 inhibitor peptide inhibits PPIA up-regulation, enhances cytokine production, and significantly enhances survival. In addition, the CD200 inhibitor results in tumor regression and enhanced survival benefit in our canine model. Impact: We are the first to correlate CD200 in brain tumors and tumor-derived vaccines as an inhibitor of immune activation. Our data suggest that we are suppressing the immune system with the same vaccines designed specifically to induce an anti-tumor response. Tumor endothelial expression of CD200 is also a likely reason for escape from native immune surveillance and failure of other immunotherapeutic approaches. We are optimistic that use of our competitive inhibitor peptide against CD200 and anti-CD200R antibody will ultimately lead to the development of novel therapeutics that improves the efficacy of cancer immunotherapy.

Biography

Michael R Olin has completed his PhD from the University of Minnesota in 2006 and Post-doctoral studies in the Department of Medicine. He has dedicated his efforts to developing immunotherapy for brain tumors. He, among others, has utilized tumor cells as vaccine components, demonstrating promising results with minimal toxicity. He has published more than 20 papers in reputed journals.

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