to activate the "type 1" inflammatory response can be implemented. Enhancing the endogenous immune response by deactivating the ensuing chronic inflammatory tumor microenvironment might provoke an immune response potent enough to activate and mobilize endogenous CTL and NK cells to eliminate the threat posed by high-grade cancerous masses.

CONCLUSION

It has long been held that tumor cells outwit the host's defenses by altering their own cellular signaling pathways. The pathway exploited to achieve malignancy may be a combination of unique derivations. Gliomas are known to exhibit compensatory activity in that when supplied with selective pressure from one treatment, they readily adapt with other mutations to survive. Other mounting evidence now suggests that some of the pathways exploited by cancer cells adopt a more malignant phenotype and are simply responses to the stimuli created by the rapidly dividing tumor cells rather than novel re-circuited pathways exploited by neoplastic cells for growth. One of the crucial responses facilitating and nurturing cancerous transformation is inflammation. A chronically active inflammatory microenvironment provides the developing cancerous mass with proliferative and mutational factors necessary to realize "self-sufficiency". It is evident that some tumors can bypass this "nurturing stage" as might be expected with primary GBM. Regardless, once this "self-sufficiency" is realized, the tumor is able to survive outside of the cancer stem cell niche. Empowered with constant proliferative cues the tumor mass divides uncontrolled. The increased proliferation results in necrosis and the resultant environment is skewed more strongly towards the Th2 inflammatory response. Thus, for high-grade gliomas a higher Th2/Th1 cytokine ratio supports the production of other immunosuppressive factors. To mount a successful cytotoxic anti-tumor response, it is crucial to restore a balanced Th2/Th1 cytokine ratio of 1:1 or less. This should decrease the proliferative rate of the tumor mass as well, since it is the Th2 response that ultimately works with the tumor cell to drive the angiogenic response. Ultimately, successful brain tumor immunotherapy should leave patients with intact immunosurveillance function and the ability to enact a cell-mediated response in the event of recurrence.

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