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### Tumor necrosis-initiated complement activation stimulates proliferation of medulloblastoma cells

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**Objective:** While the ascribed role of complement has generally been limited to inflammation and the immune response to pathogens, recent data suggest that the system has far broader functions, including that of a proliferation signal. We sought to determine the effect of necrosis-induced activation of the complement protein C3 in medulloblastoma.

**Materials/Methods:** Twelve medulloblastoma surgical specimens were evaluated for complement activation using immunohistochemistry, with H&E stains performed on adjacent tissue sections to determine the relationship of complement activation to necrotic tissue. Flow cytometry and Western blot were performed on 3 established medulloblastoma lines and 1 surgically procured cell culture to determine expression of C3a receptor (C3aR) in medulloblastoma. *In vitro* proliferation of siRNA C3aR knockdown cells was compared to that of control siRNA cells with cell line Daoy.

**Results:** Three surgical specimens were found to have necrosis on H&E sections. In each case, iC3b staining was identified on adjacent sections, limited to the necrotic region. In no case did necrosis occur without iC3b staining on adjacent sections. C3aR protein was demonstrated on both the 3 established cell lines and on the surgical culture. Proliferation assays of Daoy cells with siRNA knockdown vs. control siRNA revealed significantly reduced proliferation at 72 hours ( $p = 0.001$ ).

**Conclusions:** Necrosis is associated with complement activation in medulloblastoma. Medulloblastoma cells express C3aR, and siRNA-mediated knockdown of C3aR inhibits proliferation of these cells *in vitro*.

#### Biography

Sughrue is the current director of the comprehensive brain tumor center at the University of Oklahoma. He attended medical school at Columbia University before completing his neurosurgery residency at UCSF. He performs over 400 operations for brain tumors annually in addition to numerous active research efforts in brain tumor treatment. He has authored over 140 peer reviewed publications in addition to editing several text books.

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