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# Intra-Tumoral Injection of SS1P Immunotoxin Combined with Anti-CTLA-4 Induce Massive Local Inflammation that Eradicates Resistant Multi-Centric Murine Cancer

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**Background:** SS1P is an immunotoxin against mesothelin. Here we evaluated if SS1P injected directly into tumorscan transform tumors into living source of antigens that boost the effect of anti-CTLA-4.

**Method:** A BALB/c breast cancer cell line was transfected with human mesothelin (66C14-M) and injected in two different locations. SS1P was injected directly into one tumor loci and anti-CTLA-4 administered IP.

**Result:** In mice treated with anti-CTLA-4 and SS1P, we observed complete tumor regressions in 26 out of 30 SS1P injected tumors (87%) and in 16 out of 30 distant un-injected tumors (53%). No tumor regressions were observed in mice treated with the drugs separately supporting the case for synergic anti-tumor effect. Pathological evaluation showed a central abscess forming in injected tumors that was more prominent in combination treated mice. Surrounding the abscess, a collar of inflammation emerged only in combination treated mice containing a mixture of lymphocytes and mononuclears. Additionally, injected tumors were harvested in few time points demonstrating a time dependent increase in CD8+ cells located mainly in the inflammation collar. Furthermore, analyzing combination treated tumors showed that out of 768 immune related gene transcripts tested, 385 were elevated by twofold or more including CD8a, PDL2 and IL1 alfa (by a factor of 13, 21 and 27 respectively). Importantly, tumors from combination treated mice were tested negative for bacteria indicating that the massive inflammation found was targeting cancer cells.

**Conclusion:** Altogether, combining local SS1P with anti-CTLA-4 promotes massive inflammation that results in cure of multicentered cancer disease providing a strong rational to explore this combination therapy in patients.

**Biography:**

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