These results support our hypothesis that localized delivery of IL-12 is well tolerated as no change in clinical signs or body weight of mice treated with Ad or AL alone was observed. Moreover, this therapeutic strategy appears to be well-tolerated as no increase in IL-12 protein expression was observed in tumor tissues from mice treated with Ad-RTS-mIL-12 (Ad), administered intratumorally under the control of the Rab9 switch. However, in a recent study using HT1080 human fibrosarcoma cells transduced with AL and incubated with AL, these cells showed a dose-dependent increase in IL-12 protein with an increase in expression of 1.1 fold at 10 mg/m2 dose. In contrast, HT1080 tumor cells transduced with AL and incubated with Ad, AL showed a dose-dependent increase in IL-12 protein with an increase in expression of 1.2 fold at 10 mg/m2 dose. Therefore, from these results we conclude that a single intratumoral injection of Ad combined with peripheral injection of AL can be well-tolerated in the absence of any toxicity.

The Immune System: A controllable promoter to confer localized transcriptional foci is required. In this case, the protein heterodimer changes to a stable conformation and binds locally to the promoter.