IgE is a key player in anti-parasitic immunity and allergies. Several research groups found that IgE may exert powerful anti-tumor potency in vivo, opening a new field of investigation named AllergoOncology. Our previous studies on IgE adjuvanticity in anti-tumor vaccination, and epidemiological data suggesting an inverse association between allergy and cancer, directed our attention towards a possible role played by endogenous IgE in tumor surveillance. High IgE producer mice (KN1) immunized with irradiated TS/A-LACK mammary tumor cells are completely resistant to tumor growth after challenges with living tumor cells. This result was confirmed using N2C cells, a HER2/neu-expressing tumor model, where the lack of tumor growth has been shown even in absence of tumor immunization. In order to prove the endogenous IgE involvement in this anti-tumor protection, we created a new double mutant high IgE producer and FcɛRIα ko mouse, where, as expected, we observed tumor growth due to the inability of IgE to exert its effect in the absence of FcɛRI. Furthermore, we have direct evidence of the presence of tumor-specific IgE in the sera of high IgE producer mice, due to the activation of FcɛRI in a mediator release assay.