Epidermal growth factor receptor (EGFR) is an attractive therapeutic target due to its overexpression in ~60% of glioblastoma patients and promotion of gliomagenesis. However, expression of EGFR on normal tissue limits targeting by human T cells modified to express chimeric antigen receptors (CARs) due to potential for deleterious toxicity from recognition of normal cells. Because EGFR is expressed at a higher density on glioblastoma relative to normal tissue, we sought to generate EGFR-specific CAR+ T cells capable of distinguishing malignant from normal cells based on the disparate density of EGFR expression. This was accomplished by generating two EGFR-specific CARs from monoclonal antibodies which differ in affinity. T cells expressing Nimo-CAR, derived from lower affinity nimotuzumab (Kd = 2.1x10^-8), exhibited effector functions that directly correlated with EGFR expression density, resulting in selective targeting of high density EGFR and diminished effector response to low density EGFR, including normal human renal cortical epithelial cells. Effector response of Nimo-CAR+ T cells was not enhanced by increased duration of interaction with low density EGFR. In contrast, the activation of T cells bearing Cetux-CAR, derived from higher-affinity cetuximab (Kd = 1.8x10^-9), was not impacted by the density of EGFR expression. Furthermore, Cetux-CAR+ T cells exhibited enhanced downregulation of CAR following interaction with EGFR relative to Nimo-CAR+ T cells, which resulted in impaired effector response to rechallenge with EGFR. In an in vivo intracranial xenograft murine model of glioblastoma, Nimo-CAR+ T cells demonstrated similar inhibition of growth as Cetux-CAR+ T cells when xenografts expressed high density EGFR (340,000 receptors/cell), but showed reduced activity in response to xenografts expressing EGFR at a low density consistent with normal tissue expression (40,000 receptors/cell). In summary, we describe the generation of CARs able to tune T-cell activity to enable T cells to distinguish malignant glioblastoma cells from non-malignant cells based on EGFR expression density.