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Inflammatory chemokines are instrumental players in cancer-related inflammation contributing to numerous steps during tumor progression. In Kaposi's sarcoma, we have found that downregulation of the atypical chemokine receptor 2 (ACKR2) by the KRAS/BRAF/ERK pathway profoundly affects the tumor microenvironment, unleashing accumulation of tumor-associated macrophages that sustains tumor growth. This discovery extends our understanding on the role of inflammatory chemokines in tumor biology and provides rationale for their therapeutic targeting.