BET inhibitor suppresses neutrophil-dependent lung metastasis of inflammatory renal cancer cells

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Advanced clear cell renal cell carcinoma (ccRCC) frequently causes systemic inflammation. In the present study, the functional role and regulatory mechanism of inflammation driven by advanced ccRCC cells were identified. The inflammatory nature of advanced ccRCC was recapitulated in a preclinical model of ccRCC. Amplification of cancer cell-intrinsic inflammation during ccRCC progression triggered neutrophil-dependent lung metastasis. Massive expression of inflammation-related genes was transcriptionally activated by epigenetic remodelling through mechanisms, including super-enhancer formation. Bromodomain and extra-terminal motif inhibitor (BETi) synchronously suppressed C–X–C-type chemokines in ccRCC cells and decreased neutrophil-dependent lung metastasis. Overall, our findings shed insight into the nature of inflammatory ccRCC, which triggers metastatic cascades, and suggest a potential therapeutic strategy.