Two major transcriptional regulators of carbon metabolism in bacteria are Cra and CRP. CRP is considered to be the main mediator of catabolite repression. Unlike for CRP, in vivo DNA binding information of Cra is scarce. Here we generate and integrate ChIP-exo and RNA-seq data to identify 39 binding sites for Cra and 97 regulon genes that are regulated by Cra in *Escherichia coli*. An integrated metabolic-regulatory network was formed by including experimentally-derived regulatory information and a genome-scale metabolic network reconstruction. Applying analysis methods of systems biology to this integrated network showed that Cra enables optimal bacterial growth on poor carbon sources by redirecting and repressing glycolysis flux, by activating the glyoxylate shunt pathway, and by activating the respiratory pathway. In these regulatory mechanisms, the overriding regulatory activity of Cra over CRP is fundamental. Thus, elucidation of interacting transcriptional regulation of core carbon metabolism in bacteria by two key transcription factors was possible by combining genome-wide experimental measurement and simulation with a genomicscale metabolic model.