Chou et al found that the lack of CCR5 or CCL5 in mice impaired regulation of energy metabolism in hypothalamus. Immunostaining and co-immunoprecipitation revealed the specific expression of CCR5, associated with insulin receptors, in the hypothalamic arcuate nucleus (ARC). Both ex vivo stimulation and in vitro tissue culture studies demonstrated that the activation of insulin, and PI3K-Akt pathways were impaired in CCR5 and CCL5 deficient hypothalamus. The inhibitory phosphorylation of insulin response substrate-1 at Ser302 (IRS-1S302) but not IRS-2, by insulin was markedly increased in CCR5 and CCL5 deficient animals. Elevating CCR5/CCL5 activity induced GLUT4 membrane translocation and reduced phospho-IRS-1S302 through AMPKα-S6 Kinase. Blocking CCR5 using the antagonist, MetCCL5, abolished the de-phosphorylation of IRS-1S302 and insulin signal activation. In addition, intracerebroventricular delivery of MetCCL5 interrupted hypothalamic insulin signaling and elicited peripheral insulin responsiveness and glucose intolerance. Taken together, our data suggest that CCR5 regulates insulin signaling in hypothalamus which contributes to systemic insulin sensitivity and glucose metabolism [1)].

In a study, Wang et al., analyzed the effects of hypoxia and macrophages on invasion of GBM cells and its potential mechanisms. They found that both hypoxia and macrophage supernatant promoted GBM cells invasion and matrix metalloproteinase (MMP)-9 expression, and hypoxia modulated the invasive activity of GBM cells by upregulating their CCR5 expression. The supernatant of hypoxic macrophages also showed greater pro-invasion effect than normoxic macrophages through the elevated secretion of CCL4. Moreover, they found that interferon regulatory factor-8 (IRF-8) was possibly involved in hypoxia-modulated CCL4 expression of macrophages. Taken together, the present study found that macrophages promoted GBM invasion by the CCL4-CCR5 axis, and hypoxia enhanced the interaction between these two types of cells by upregulating both CCL4 and CCR5 expression, respectively. The results of the present study suggested that hypoxia would be a potential target for the development of immune therapies of GBM [2)].

1)
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2)
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