The therapeutic application of siRNA shows promise as an alternative approach to small molecule inhibitors for the treatment of human disease. However, the major obstacle to its use has been the difficulty in delivering these large anionic molecules \textit{in vivo}. In this transaction, we review our recent investigations of siRNA-mediated knockdown of p38 MAP kinase mRNA in mouse lung following conjugation to the cell penetrating peptides, Tat and penetratin. Administration of siRNA into mouse lungs resulted in localisation within macrophages and scattered epithelial cells and produced knockdown of p38 MAP kinase mRNA. However, siRNA conjugation to penetratin and TAT had no effect upon either the magnitude or duration of p38 MAP kinase knockdown. Importantly, administration of the penetratin or Tat(48-60) peptides alone influenced p38 MAP kinase mRNA expression whilst the penetratin-siRNA conjugate activated the innate immune response. At the present time, these studies suggest that cell penetrating peptides would not appear to be of utility for siRNA delivery into mouse lung.