

# Leveraging genetic data to investigate the effects of interleukin-6 receptor signalling on levels of 40 circulating cytokines.

Rezbiara Rahman<sup>1</sup>, Lauren McEwan<sup>1</sup>, David Ryan<sup>2</sup>, and Dipender Gill<sup>2</sup>

<sup>1</sup>St George's University of London

<sup>2</sup>St George's University Hospitals NHS Foundation Trust

June 23, 2021

## Abstract

Abstract Interleukin 6 (IL-6) is a circulating cytokine that is implicated in a range of inflammatory diseases. However, the broad effects of IL-6 receptor (IL-6R) signalling on other circulating cytokines is not known. Using summary-level data from genome-wide association studies, we leveraged genetic variants that proxy IL-6R signalling in two-sample Mendelian randomization analyses to investigate effects on levels of 40 circulating cytokines. Increased genetically proxied IL-6R signalling was associated with reduced levels of 10 circulating interleukins, chemokines, and growth factors. The findings from this study support feedback effects of IL-6R signalling on reducing levels of a range of circulating cytokines and identify compensatory mechanisms that may be modulating its inflammatory effects. These results provide novel insight into the mechanisms by which IL-6R signalling may be contributing to inflammatory and autoimmune diseases.

## Hosted file

MANUSCRIPT IL6R.docx available at <https://authorea.com/users/421390/articles/527446-leveraging-genetic-data-to-investigate-the-effects-of-interleukin-6-receptor-signalling-on-levels-of-40-circulating-cytokines>