**Introduction**

Drug-drug interactions involving therapeutic proteins that can modulate effects of cytokines and potentially induce changes in the enzymes (P450s) and transporters (e.g., MDR1) that are involved in drug metabolism and/or transport has been an issue of increasing interest to regulatory agencies and pharmaceutical industry sponsors in recent years. The well-documented therapeutic protein inhibition of oxidizing enzymes is of concern not only in populations where hypothyroidism (e.g., infants) or diabetes (e.g., insulin) or patients with liver disease (e.g., cirrhosis) are more prevalent, but also in patients with diseases that inhibit the activity of drug metabolizing enzymes. As an example, chronic hepatitis C virus infection has been associated with a decreased in vivo hepatic activity of drug metabolizing enzymes such as CYP2C19.

**Materials & Methods**

Chloroquine and mephenytoin: TV-1106, mephenytoin, and chloroquine were used to examine drug-drug effects of therapeutic proteins on drug metabolism. The chloroquine and mephenytoin were used as probe substrates for CYP1A2 and CYP2C19, respectively. The chloroquine and mephenytoin were added to the cell culture medium at a concentration of 25 μM and 50 μM, respectively. After 30-min incubation with these probe substrates, the cell culture medium was harvested and analyzed for the levels of chloroquine and mephenytoin by LC-MS/MS.

**Results**

**Conclusions**

We compared TV-1106, an albumin-fused GH, and recombinant human GH activity to stimulate cytokine secretion in whole blood and the effects of the drugs on the expression of cytokine mRNA and protein levels. We found that GH-induced cytokine secretion in whole blood was similar to that of the recombinant human GH in vitro.

**References**