

MATERNAL COVID-19 MAY NEGATIVELY INFLUENCE TROPHOBLAST CELL FUNCTION

Milica Jovanović Krivokuća¹, Aleksandra Vilotić¹, Danica Čujić¹

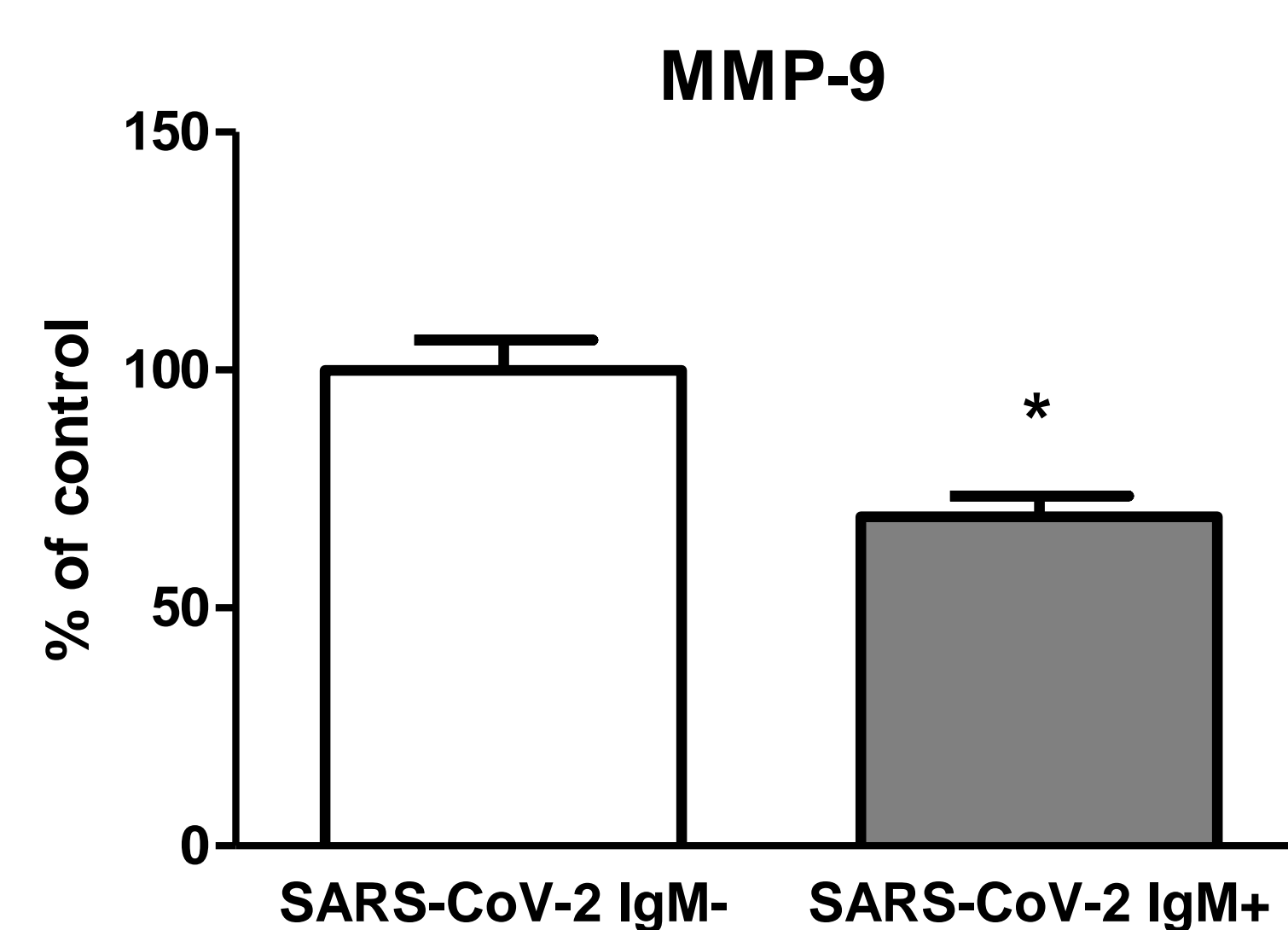
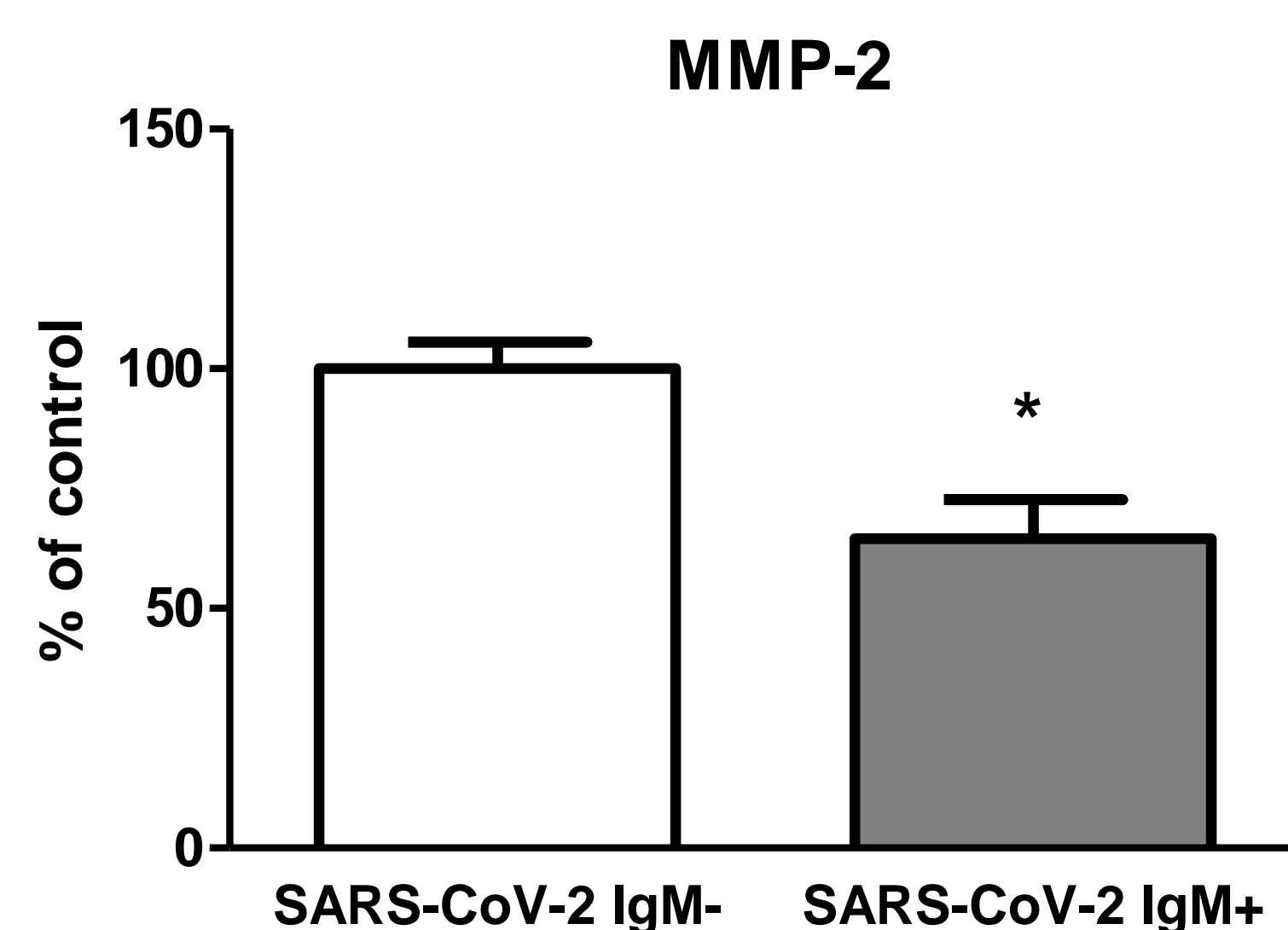
¹Institute for Application of Nuclear Energy, INEP, University of Belgrade, Belgrade, Serbia

Introduction

Coronavirus disease, COVID-19, caused by SARS-CoV-2 virus is ongoing global problem. It has been shown that pregnant women are at greater risk for a severe illness. Moreover, the infection may lead to the massive placental damage i.e. trophoblast necrosis and inflammation. SARS-CoV-2 infection is also proposed to be a risk factor for early pregnancy loss. Extravillous trophoblast cells are specific cells of the placenta that invade maternal uterine tissue and are in direct contact with maternal circulation. Trophoblast invasion is essential process for the establishment and maintenance of pregnancy, while matrix metalloproteinases (MMP) -2 and -9 are among crucial molecular mediators.

This pilot study was designed to investigate the possible effects of maternal sera obtained within three months from COVID-19 on the trophoblast cell function. Sera from eight women of reproductive age positive for IgM towards SARS-CoV-2 were used to treat extravillous trophoblast cell line HTR-8/SVneo. Sera from healthy age-matched women were used as control.

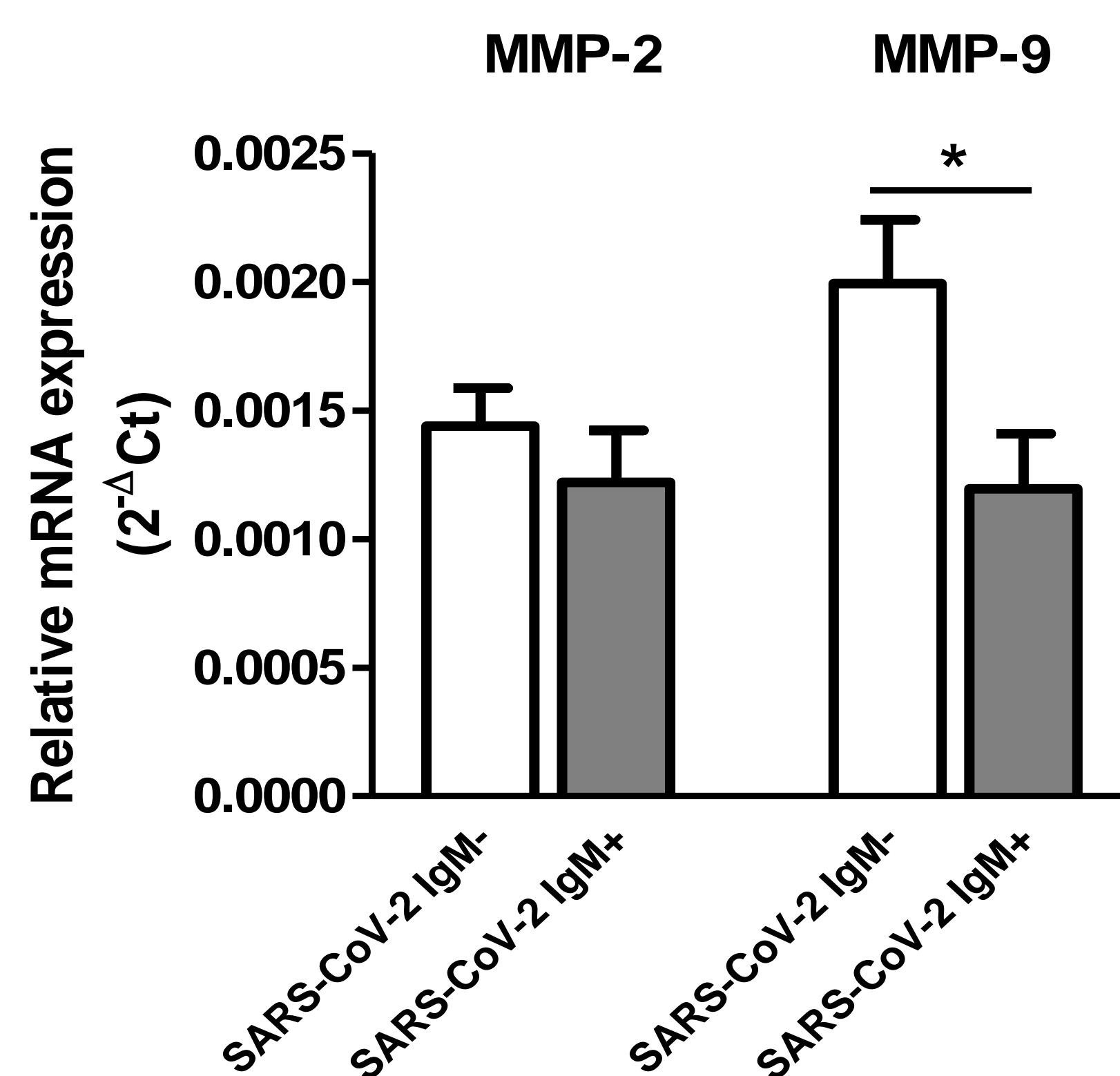
Results



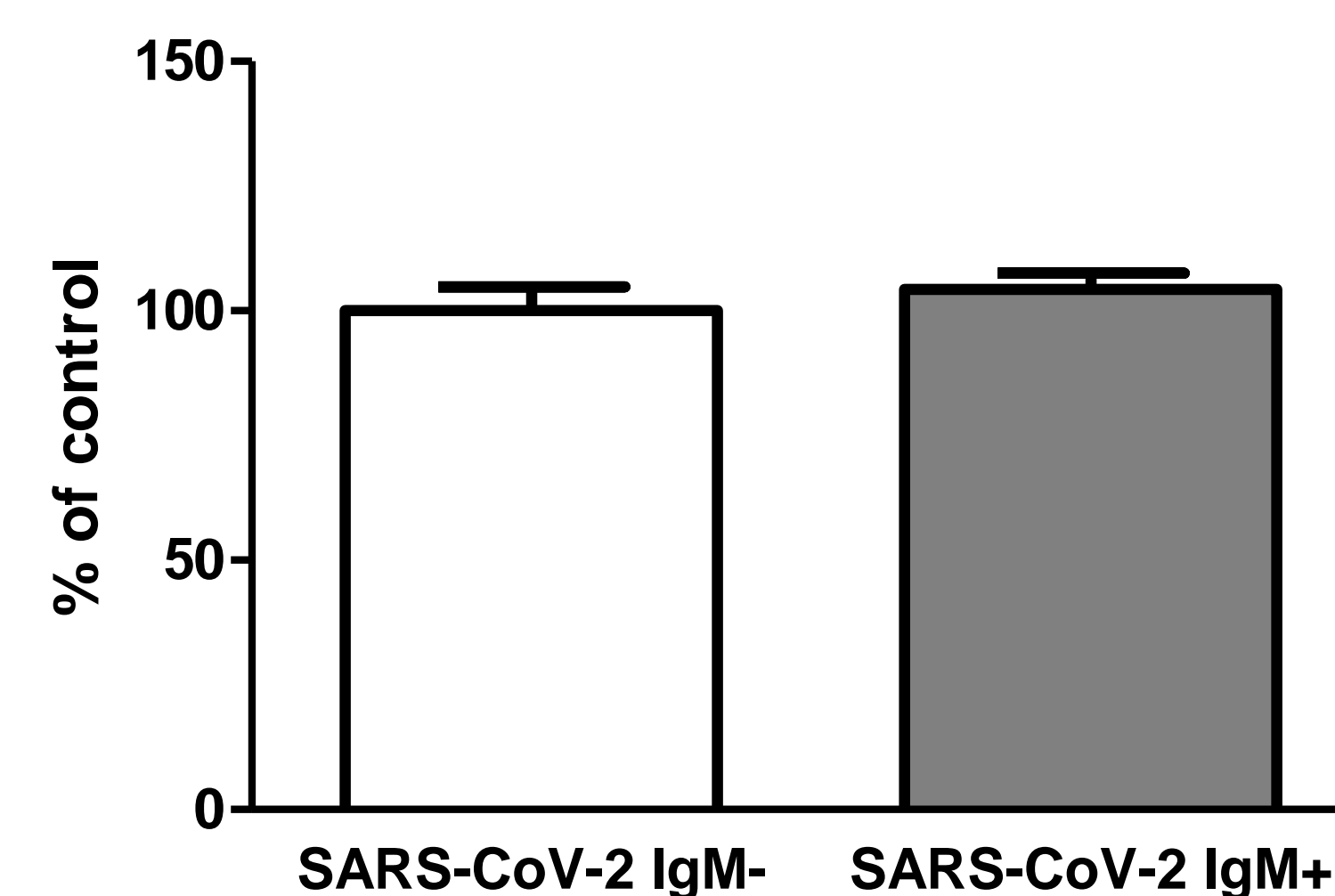
The effect of SARS-CoV-2 IgM+ serum on the levels of MMP-2 and MMP-9 in HTR-8/SVneo cell lysates following 24h of treatment. Data are expressed as mean+SEM. *p<0.05

Material and methods

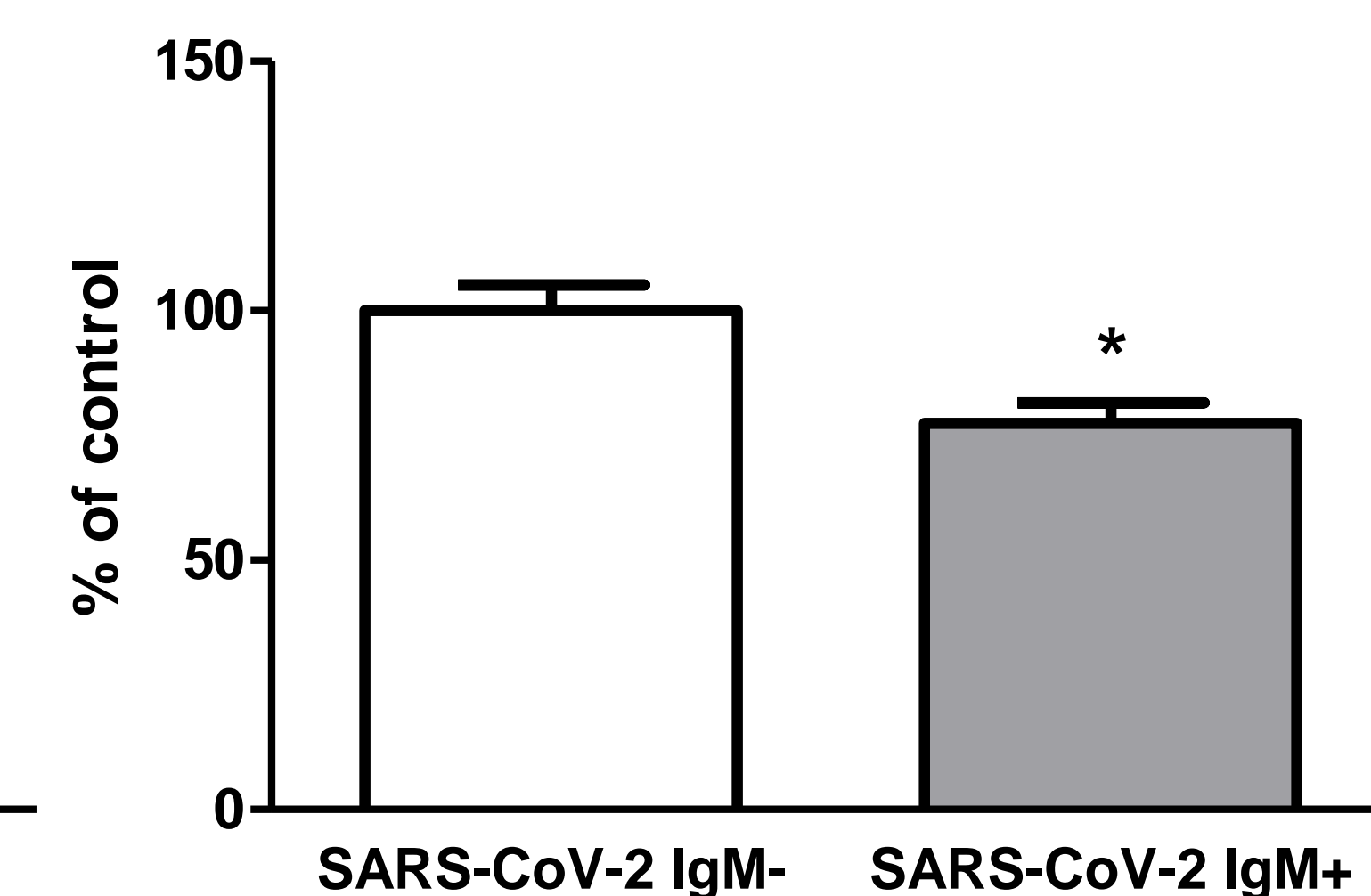
- Cells- Extravillous trophoblast cell line HTR-8/SVneo derived from first trimester placental tissue explants was used as a model
- HTR-8/SVneo cells were treated for 24 h with 5% SARS-CoV2 IgM- or IgM+ serum
- Cell viability was assessed by MTT assay
- Cell migration was measured using a wound healing „scratch“ assay
- The expression of MMP-2 and MMP-9 at mRNA level was assessed by qPCR
- Relative protein levels of MMP-2 and MMP-9 in HTR-8/SVneo cell lysates were determined by SDS-PAGE gelatin zymography



The effect of SARS-CoV-2 IgM+ serum on MMP-2 and MMP-9 mRNA expression in HTR-8/SVneo cells after 24h of treatment. Data are expressed as mean+SEM. * p<0.05



The effect of SARS-CoV-2 IgM+ serum on HTR-8/SVneo cell viability after 24h of treatment. Data are expressed as mean+SEM.



The effect of SARS-CoV-2 IgM+ on HTR-8/SVneo cell migration following 24h of treatment. Data are expressed as mean+SEM. *p<0.05

Conclusion

The results of this pilot study suggest the potential negative effect of maternal COVID-19 on the trophoblast cell function and hence on the placentation process which could lead to pregnancy loss or intrauterine growth restriction. However, these findings need further verification using a larger number of sera and a confirmation in vivo.