ID der Kurzfassung : **204**

Inhibition of p38 MAPK during hyperinflammatory virus infections – achievements and challenges in vivo

Inhalt

Zoonotic respiratory viruses crossing the species barrier to humans like SARS-CoV-2 or highly pathogenic avian influenza A virus (HPAIV) often lead to a rapid clinical deterioration in late disease stages, correlating with systemic hyperinflammation and requiring new immunomodulatory therapeutic approaches. We suggest that the key inflammatory MAPK p38 substantially drives the development of this immune dysregulation. Using clinically evaluated p38 inhibitors we significantly reduced the pro-inflammatory cytokine expression during SARS-CoV-2 infection *in vitro* in human lung cells and organoids as well as *ex vivo* in lung explants while maintaining the interferon-mediated antiviral response. Strikingly, we discovered a strong drug synergy between p38 inhibition and the antiviral remdesivir.

Despite of strong efficacy *in vitro* and *ex vivo*, daily application of p38 inhibitors in BALB/c and C57BL/6 mice provided controversial results. On the one hand, treatment from 72 h post infection led to exacerbation of low pathogenic influenza A virus infection. On the other hand, survival as well as pathogenesis during SARS-CoV-2 or HPAIV infection were not significantly affected by treatment from day of infection.

This work discusses p38 inhibition as promising therapeutic approach for hyperinflammatory virus infections and how to overcome the investigatory hurdle from *in vitro*/ *ex vivo* drug applications to *in vivo*, considering mouse models, drug applications and solvents.

Keywords

Zoonotic viruses, SARS-CoV-2, Influenza A Virus, inflammation, treatment approaches, p38 MAPK

Registration-ID code

ZOO23-461

Professional Status of the Speaker

Postdoc

Junior Scientist Status

Yes, I am a Junior Scientist.

Thema Einordnung: Pathogenesis & Pathology of Zoonotic Infections

Typ des Beitrags: Poster presentation