

SARS-CoV-2 induces vital NET formation independent of available oxygen

Inhalt

During COVID-19, neutrophils are activated and massively release neutrophil extracellular traps (NETs), contributing to disease severity. Yet, the exact mechanism of NET formation is not fully understood. Since patients suffer from acute hypoxia during severe cases, it is necessary to study neutrophil biology at low oxygen level. Thus, we compared NET formation of human neutrophils as response to recombinant SARS-CoV-2 viral proteins under hypoxia and normoxia (1 - 21 % O₂). Calprotectin was quantified in cell culture supernatant and found to be significantly increased by stimulation with spike protein under both oxygen conditions, while cell death marker LDH remained unaltered. Vesicular structures with positive NET marker signals were observed during confocal microscopy, indicating a vital form of NET formation, rather than cell death-linked NETosis. Electron microscopy confirmed that NET-packed vesicles were formed in the neutrophils by stimulation with spike protein. Additionally, in vivo samples were collected from SARS-CoV-2 infected hamsters at 6 days post infection. Here, lung tissue shows clear signs for hypoxia by positive staining for hypoxia inducible factor. In good correlation to the in vitro data, bronchoalveolar lavage fluid of SARS-CoV-2 infected hamsters showed similar NET-vesicles as found in response to spike protein in vitro. In conclusion, this is the first report of a vesicular NET-release as response to SARS-CoV-2-infections under hypoxic conditions.

Keywords

NET formation, SARS-CoV-2, Hypoxia

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Professional Status of the Speaker

Postdoc

Junior Scientist Status

Yes, I am a Junior Scientist.

Thema Einordnung: Host-pathogen Interactions

Typ des Beitrags: Both Options Possible