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| |  |  | | --- | --- | | Title: | **Repurposing the antimalarial compound artemisinin as a novel therapy for inflammatory conditions** | | Authors: | Hassan Morad - *King's College London*, *United Kingdom*; Suaib Luqman - *Central Institute of Medicinal and Aromatic Plants*; Larissa Garcia-Pinto - *King's College London*; Kevin Cunningham - *King's College London*; Bruno Vilar - *King's College London*; Georgia Clayton - *King's College London*; Manu Shankar-Hari - *King's College London*; Peter McNaughton - *King's College London* | | Session: | [Session one](https://www.eventsforce.net/biochemsoc/system/proweb/start.csp?pageID=64614&eventID=130) - Default Location, 10/05/2022, 13:00 - 14:30 | | Time: | 14:15 - 14:30 | |
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| |  | | --- | | Immune cell chemotaxis to sites of pathogen invasion is critical for fighting infection, but in life-threatening conditions such as sepsis and Covid-19, excess activation of the innate immune system is thought to cause a damaging invasion of immune cells into tissues and an excessive release of cytokines. In these circumstances, tempering excessive activation of the innate immune system may, paradoxically, promote recovery. Here we describe the repurposing of the antimalarial compound artemisinin towards a novel treatment for inflammatory conditions characterised by over-activation of the innate immune system. We identify artemisinin (and its analogue artesunate) as a potent inhibitor of neutrophil and macrophage chemotaxis. Artemisinin released calcium from intracellular stores by inhibiting isoform-3 of Sarcoplasmic/Endoplasmic Reticulum Calcium Atpase (SERCA3). Inhibition was irreversible and inhibited by iron chelation, suggesting iron-catalysed alkylation of SERCA3 as the mechanism by which artemisinin inhibits immune cell motility. In murine infection models, artemisinin/artesunate potently suppressed innate immune cell invasion into both peritoneum and lung and inhibited the release of cytokines/chemokines and neutrophil extracellular traps (NETs). This work suggests that artemisinin and artesunate may have value as therapies in conditions such as sepsis and Covid-19 in which over-activation of the innate immune system causes tissue injury that can lead to death. From these data we proposed a clinical trial of artesunate for Covid-19 patients, which the WHO accepted and are now running as part of the ‘SOLIDARITY’ initiative. | |