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Determining the role of protein aggregation in COVID-19

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COVID-19 is primarily known as a respiratory disease caused by the virus SARS-CoV-2. However, neurological symptoms such as memory loss, sensory confusion, cognitive and psychiatric issues, severe headaches, and even stroke are reported in as many as 30 % of cases and can persist even after the infection is over (so-called 'long COVID'). These neurological symptoms are thought to be caused by brain inflammation and toxicity, triggered by the virus infecting the central nervous system of COVID-19 patients, however we still don't understand the molecular mechanisms underpinning this neurotoxicity. The neurological effects of COVID-19 share many similarities to neurodegenerative diseases such as Alzheimer's and Parkinson's in which the presence of cytotoxic self-assembled protein aggregates, known as amyloid nanofibrils are a common hallmark. This led us to hypothesise that self-assembled amyloid aggregates maybe present in the proteome of SARS-CoV-2 and responsible for some of the neurological symptoms of COVID-19. In this work we identified several peptides sequences within the proteome of SARS-CoV-2 that have a strong tendency to spontaneously self-assemble into amyloid aggregates. We performed an extensive characterisation of the in vitro toxicity and biophysical properties of these assemblies using a variety of techniques. We used data recorded at the SAXS/WAXS beamline at the Australian Synchrotron to provide insights into the nanoscale morphology and molecular structure of these assemblies. Based on these results we introduce the idea that cytotoxic amyloid aggregates of SARS-CoV-2 proteins are causing some of the neurological symptoms commonly found in COVID-19 and contributing to long COVID.

Level of Expertise

Experienced Researcher

Presenter Gender

Man

Pronouns

He/Him

Which facility did you use for your research

Australian Synchrotron

Students Only - Are you interested in AINSE student funding

No

Do you wish to take part in the Student Poster Slam

No

Condition of submission

Yes

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