

α B-crystallin affects the morphology of A β (1-40) aggregates

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Manuscript Source: <https://www.biorxiv.org/content/10.1101/2021.03.07.433908v1>

Manuscript Authors: Henrik Müller, David M. Dias, Anna van der Zalm & Andrew J. Baldwin

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The combined approaches ensure easier, faster, more effective proofreading.

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- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
- Always consult the original research paper as the true reference source for the text.

Contact Information:

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All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title **α B-crystallin affects the morphology of A β (1-40) aggregates**

S1 [001] Summary

S1 [002] α B-crystallin (ABC) is a human small heat shock protein that is strongly linked to Alzheimer's disease (AD).

α B-crystallin ...
... (ABC) ...
... is a human small heat shock protein ...
... that is strongly linked ...
... to Alzheimer's disease ...
... (AD).

S1 [003] In vitro, it can inhibit the aggregation and amyloid formation of a range of proteins including A β (1-40), a primary component of AD amyloid plaques.

In vitro, ...
... it can inhibit the aggregation ...
... and amyloid formation ...
... of a range ...
... of proteins including A β (1-40), ...
... a primary component ...
... of AD amyloid plaques.

S1 [004] Despite the strong links, the mechanism by which ABC inhibits amyloid formation has remained elusive, in part due to the notorious irreproducibility of aggregation assays involving preparations of A β -peptides of native sequence.

Despite the strong links, ...
... the mechanism ...
... by which ABC inhibits amyloid formation has remained elusive, ...
... in part ...
... due to the notorious irreproducibility ...
... of aggregation assays ...
... involving preparations ...
... of A β -peptides ...
... of native sequence.

S1 [005] Here, we present a recombinant expression protocol to produce native A β (1-40), devoid of any modifications or exogenous residues, with yields up to 4 mg/L E. coli.

Here, ...
... we present a recombinant expression protocol ...
... to produce native A β (1-40), ...
... devoid ...
... of any modifications ...
... or exogenous residues, ...
... with yields up to 4 mg/L E. coli.

S1 [006] This material provides highly reproducible aggregation kinetics and, by varying the solution conditions, we obtain either highly ordered amyloid fibrils or more disordered aggregates.

This material provides highly reproducible aggregation kinetics and, ...
... by varying the solution conditions, ...
... we obtain either highly ordered amyloid fibrils ...
... or more disordered aggregates.

S1 [007] Addition of ABC slows the aggregation of A β (1-40), and interferes specifically with the formation of ordered amyloid fibrils, favouring instead the more disordered aggregates.

Addition ...
... of ABC slows the aggregation ...
... of A β (1-40), ...
... and interferes specifically ...
... with the formation ...
... of ordered amyloid fibrils, ...
... favouring instead the more disordered aggregates.

S1 [008] Solution-state NMR spectroscopy reveals that the interaction of ABC with A β (1-40) depends on the specific aggregate morphology.

Solution-state NMR spectroscopy reveals ...
... that the interaction ...
... of ABC ...
... with A β (1-40) ...
... depends ...
... on the specific aggregate morphology.

S1 [009] These results provide mechanistic insight into how ABC inhibits the formation of amyloid fibrils.

These results provide mechanistic insight ...
... into how ABC inhibits the formation ...
... of amyloid fibrils.

S1 [010] Highlights

Highlights

S1 [011] Protocol for production of native recombinant A β (1-40)

Protocol ...
... for production ...
... of native recombinant A β (1-40)

S1 [012] Amyloid formation under physiological conditions is highly reproducible

Amyloid formation ...
... under physiological conditions is highly reproducible

S1 [013] Both ordered fibrils and disordered aggregates can be reliably formed

Both ordered fibrils ...
... and disordered aggregates can be reliably formed

S1 [014] α B-crystallin specifically inhibits amyloid fibril assembling, favouring disordered aggregates

 α B-crystallin specifically inhibits amyloid fibril assembling, ...
 ... favouring disordered aggregates

S1 [015] eTOC blurb Müller et al. introduce a protocol for the highly reproducible production of amyloid from native A β (1-40) and determine that the human chaperone ABC specifically destabilises them in favour of disordered aggregates.

 eTOC blurb Müller et al. introduce a protocol ...
 ... for the highly reproducible production ...
 ... of amyloid ...
 ... from native A β (1-40) ...
 ... and determine ...
 ... that the human chaperone ABC specifically destabilises them ...
 ... in favour ...
 ... of disordered aggregates.

S1 [016] NMR shows that ABC can distinguish between aggregate morphologies.

 NMR shows ...
 ... that ABC can distinguish ...
 ... between aggregate morphologies.

S2 [017] Introduction

S2 [018] Alzheimer's disease (AD) is associated with the aggregation of amyloid- β (A β)-peptides into amyloid plaques in the brains of AD patients (Thal, et al., 2015).

 Alzheimer's disease ...
 ... (AD) ...
 ... is associated ...
 ... with the aggregation ...
 ... of amyloid- β ...
 ... (A β)-peptides ...
 ... into amyloid plaques ...
 ... in the brains ...
 ... of AD patients ...
 ... (Thal, ...
 ... et al., 2015).

S2 [019] The human small heat shock protein α B-crystallin (ABC) is up-regulated in neurons and glia adjacent to amyloid plaques (Haslbeck, et al., 2005) and is co-localised with amyloid plaques extracted from AD patients (Ecroyd and Carver, 2009).

 The human small heat shock protein α B-crystallin ...
 ... (ABC) ...

... is up-regulated ...
... in neurons ...
... and glia adjacent ...
... to amyloid plaques ...
... (Haslbeck, ...
... et al., 2005) ...
... and is co-localised ...
... with amyloid plaques extracted ...
... from AD patients ...
... (Ecroyd ...
... and Carver, 2009).

S2 [020] In-vitro, ABC prevents a range of proteins from aggregating and forming amyloid and reduces the toxic effects of amyloid on cell cultures (Hochberg, et al., 2014; Wilhelmus, et al., 2006).

In-vitro, ...
... ABC prevents a range ...
... of proteins ...
... from aggregating ...
... and forming amyloid ...
... and reduces the toxic effects ...
... of amyloid ...
... on cell cultures ...
... (Hochberg, ...
... et al., 2014; ...
... Wilhelmus, ...
... et al., 2006).

S2 [021] Despite these links, studying its mechanism has proven tremendously challenging.

Despite these links, ...
... studying its mechanism has proven tremendously challenging.

S2 [022] The principle difficulty is in obtaining reproducible kinetic data.

The principle difficulty is ...
... in obtaining reproducible kinetic data.

S2 [023] Even when isolated, ABC spontaneously adopts a polydisperse range of oligomers containing ca. 10 to 50 subunits centred on a mass of ~ 560 kDa (Hilton, et al., 2013).

Even ...
... when isolated, ...
... ABC spontaneously adopts a polydisperse range ...
... of oligomers containing ca. 10 ...
... to 50 subunits centred ...
... on a mass ...
... of ~ 560 kDa ...
... (Hilton, ...
... et al., 2013).

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