

Biglycan Attenuates Amyloid- β and Tau Pathology in iPSC-Derived Cortical Organoids from Early-Onset Alzheimer's Disease Patients

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INTRODUCTION

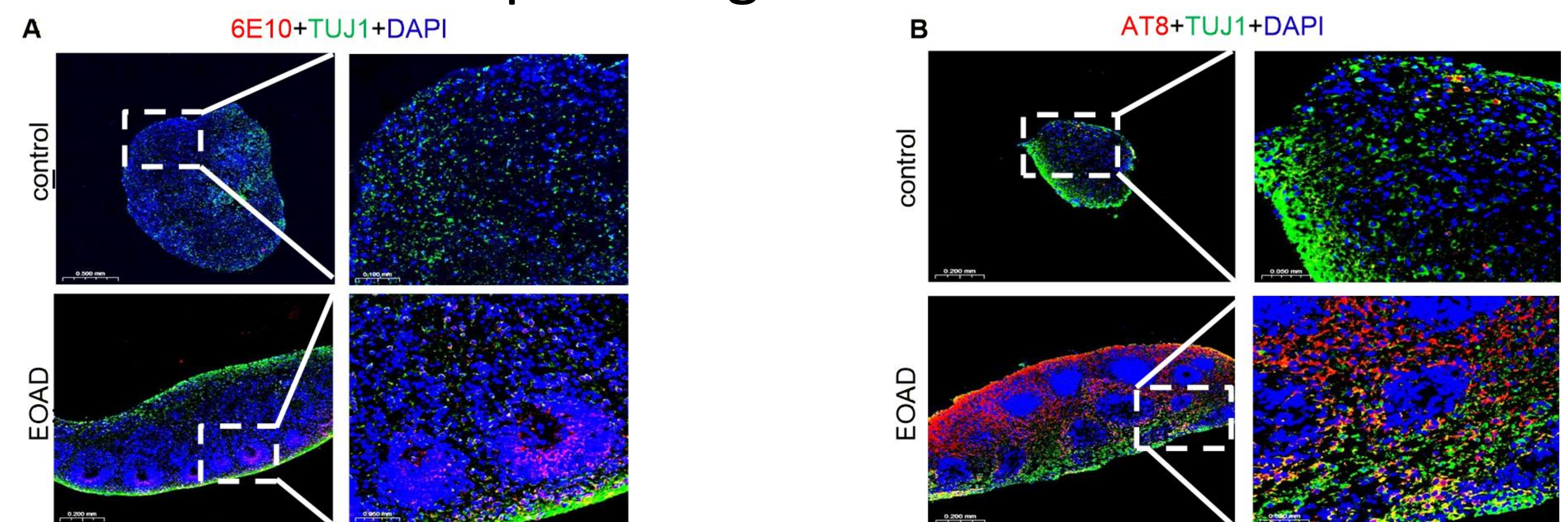
Early-onset Alzheimer's disease (EOAD) provides a powerful human genetic context to dissect disease-initiating mechanisms. Small leucine-rich proteoglycans, including Biglycan (BGN) and Decorin (DCN), have been implicated in neuroinflammation and extracellular matrix signaling, yet their roles in AD pathogenesis remain poorly defined.

METHODS

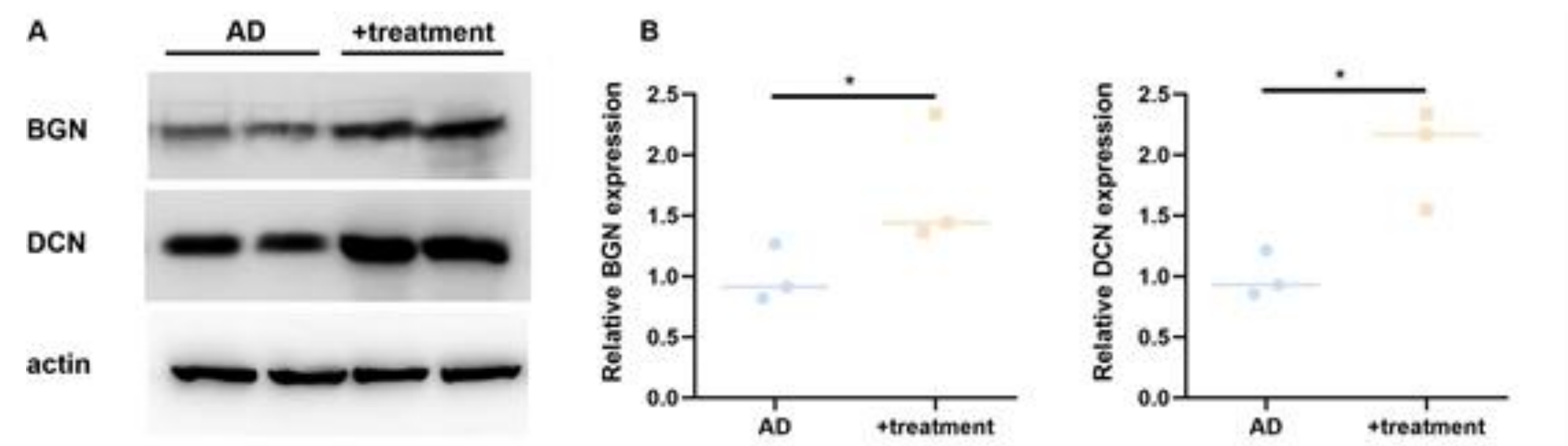
- Patient-derived and control iPSCs
- Differentiation into cortical neurons and cortical organoids
- BGN/DCN recombinant protein treatment
- ELISA: A β 42, A β 40, A β 42/A β 40
- Immunofluorescence: A β , p-tau
- Western blot

RESULTS

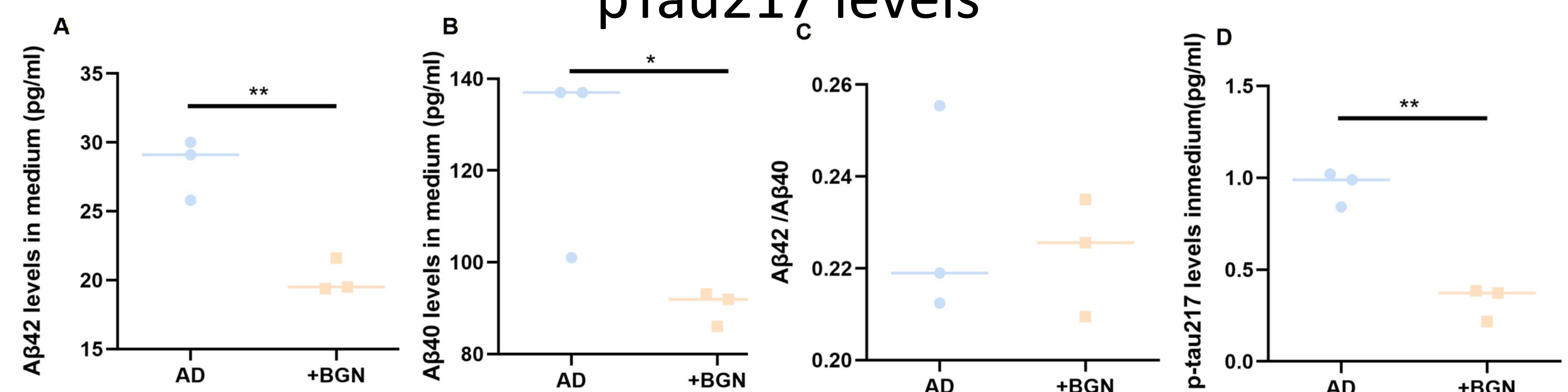
EOAD-derived cortical organoids recapitulated key AD pathological features



Overexpression of BGN and DCN



BGN overexpression markedly reduced A β 42, A β 40, and pTau217 levels



CONCLUSION

These results highlight a previously underappreciated role of extracellular matrix-associated proteoglycans in AD and suggest BGN as a potential therapeutic target.