

Age-linked Protein Damage By isoDGR-motif Drives Blood Brain Barrier (BBB) Breakdown And Cognitive Decline

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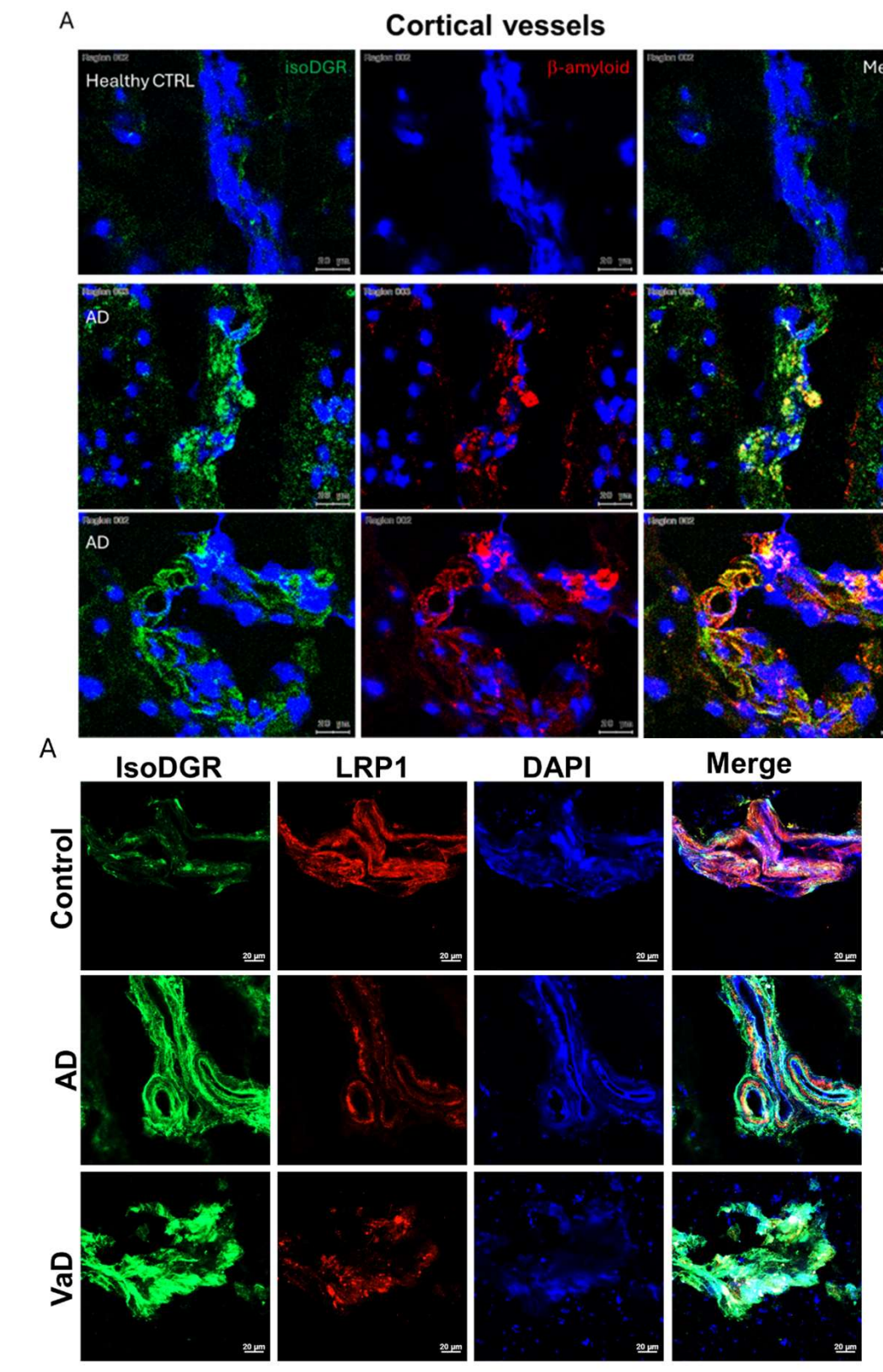
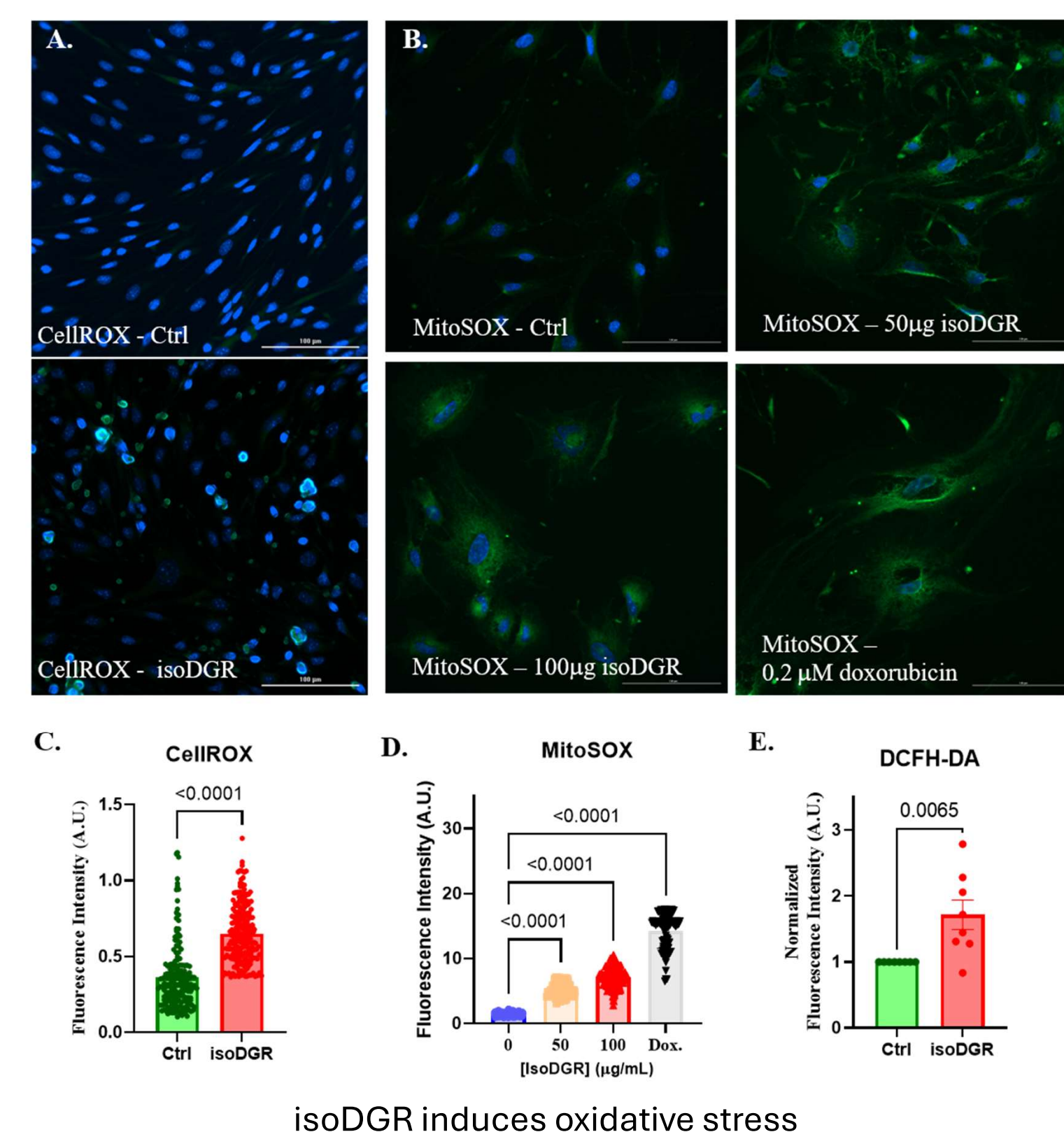
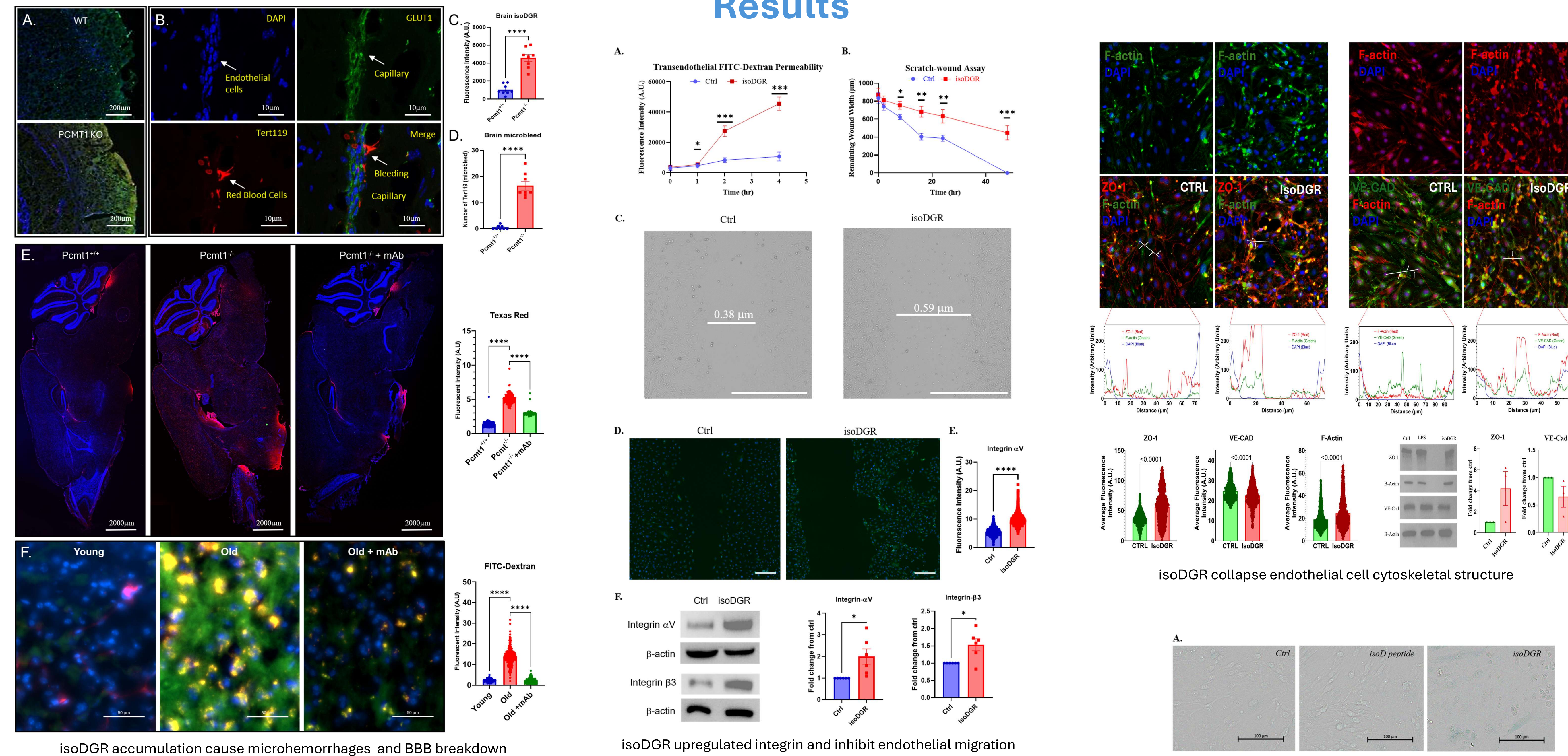
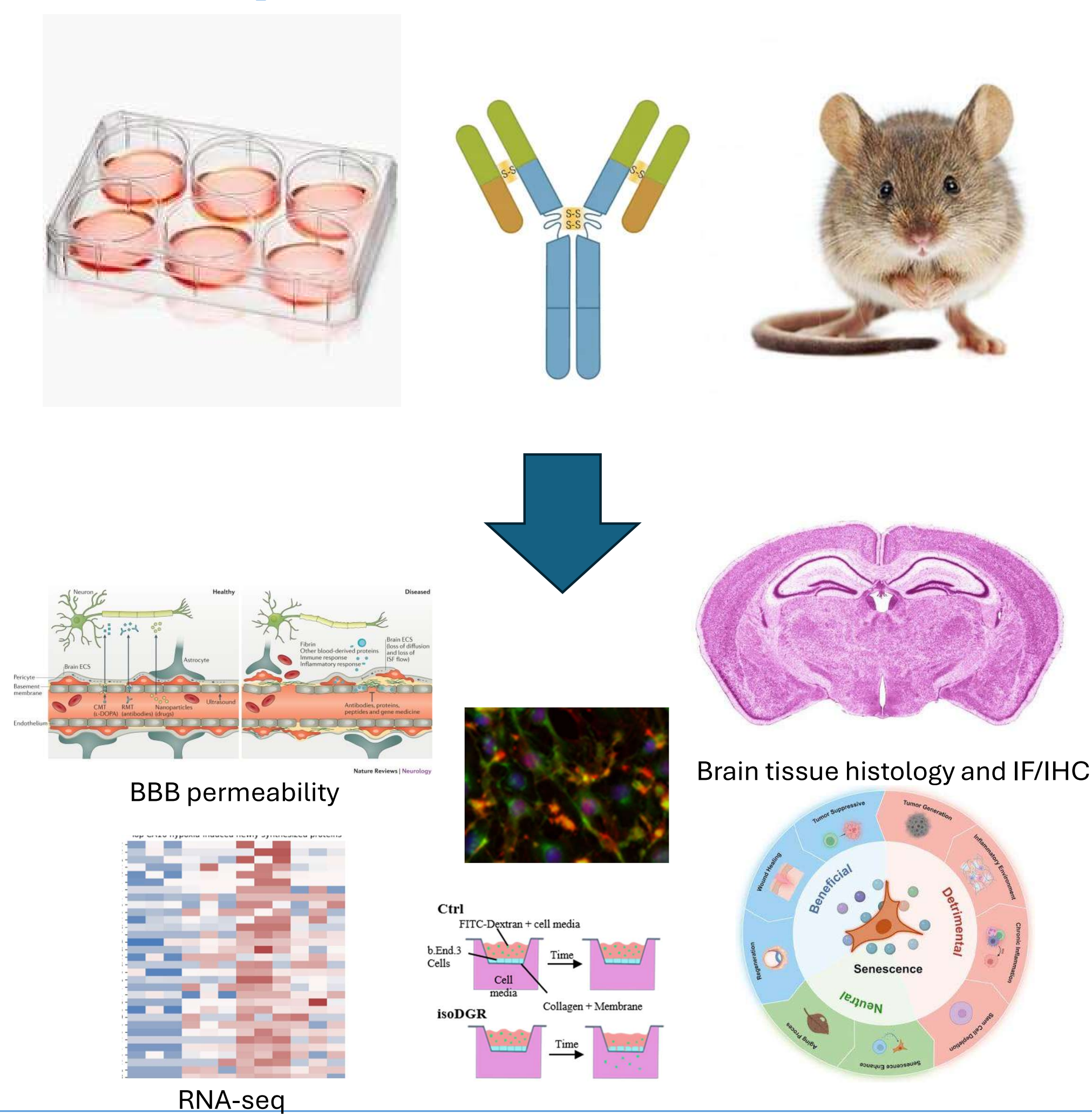
Background

- Aging is the strongest risk factor for Alzheimer's disease (AD) and vascular dementia (VaD).
- Spontaneous deamidation converts Asp-Gly-Arg (NGR) motifs into isoAsp-Gly-Arg (**isoDGR**), a gain-of-function integrin ligand that accumulates in long-lived extracellular matrix proteins.
- isoDGR accumulation in cerebral microvessels with aging and dementia.

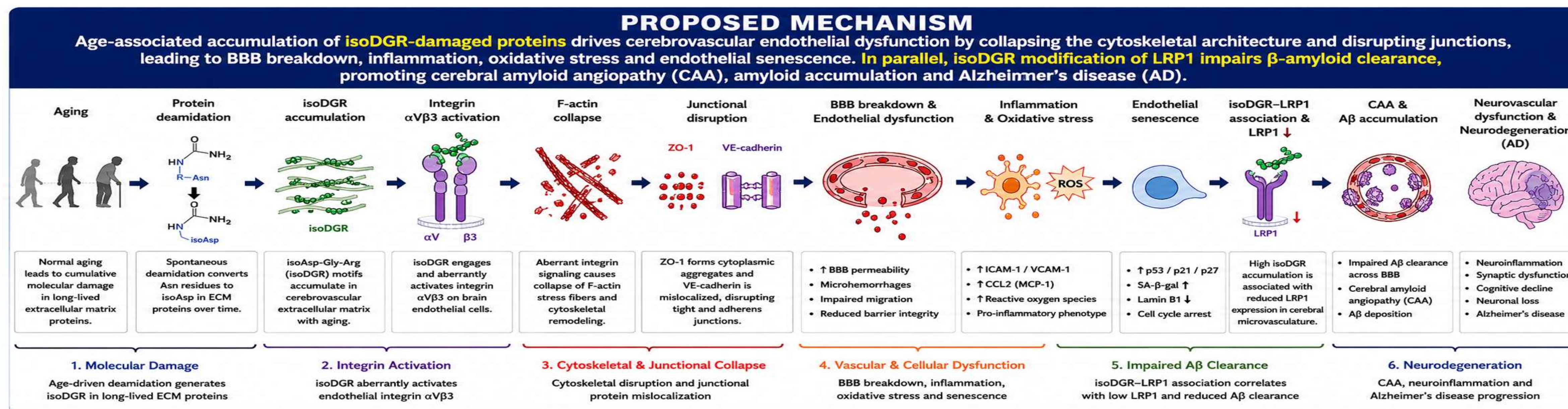
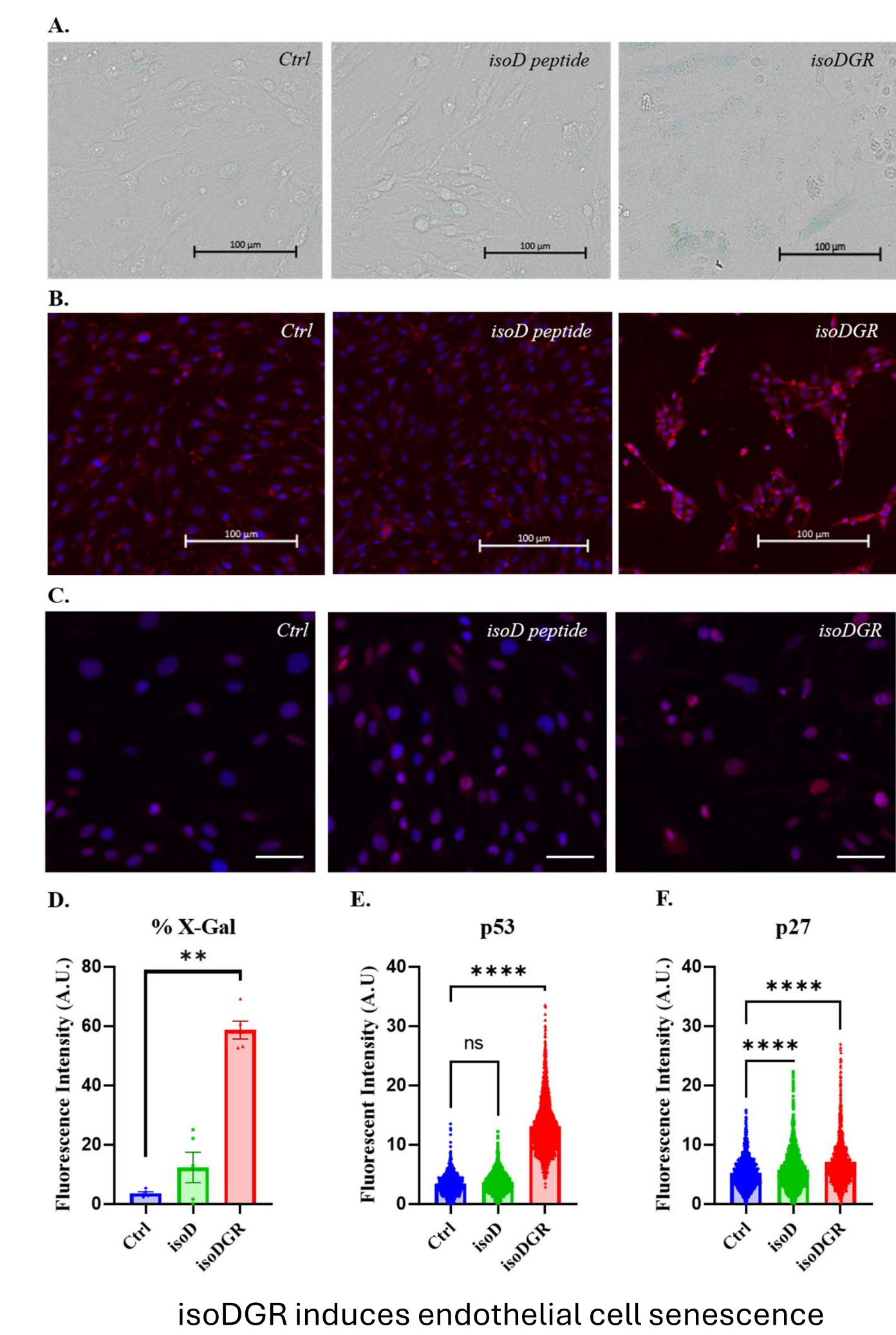
Hypothesis

Age-associated isoDGR-damaged proteins induce BBB dysfunction by disrupting endothelial cytoskeletal integrity and junctional organization. In parallel, isoDGR-modified LRP1 impairs β -amyloid clearance, promoting cerebral amyloid accumulation and Alzheimer's disease.

Experimental Overview



1. IsoDGR and β -amyloid accumulate in cortical cerebral microvessels of Alzheimer's disease patients.
2. Elevated vascular isoDGR is associated with reduced LRP1 expression, consistent with impaired β -amyloid clearance across the blood-brain barrier.



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Acknowledgements

