

Isogenic Brain Organoids for Alzheimer's Disease Research

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Introduction

- Alzheimer's disease (AD) is complex and difficult to model accurately.
- Traditional animal and 2D cell models do not fully reproduce human AD pathology.
- Brain organoids provide a 3D human model of brain development and disease.
- Organoids can differ because of donor genetic variation.
- Isogenic organoids control genetic background, allowing researchers to isolate effects of specific AD-associated variants.

Methods

- Conducted a literature review of isogenic brain organoids in AD research.
- Searched PubMed and Google Scholar for studies on AD, isogenic models, and brain organoids
- Evaluated evidence for their advantages, limitations, and research applications.

Results

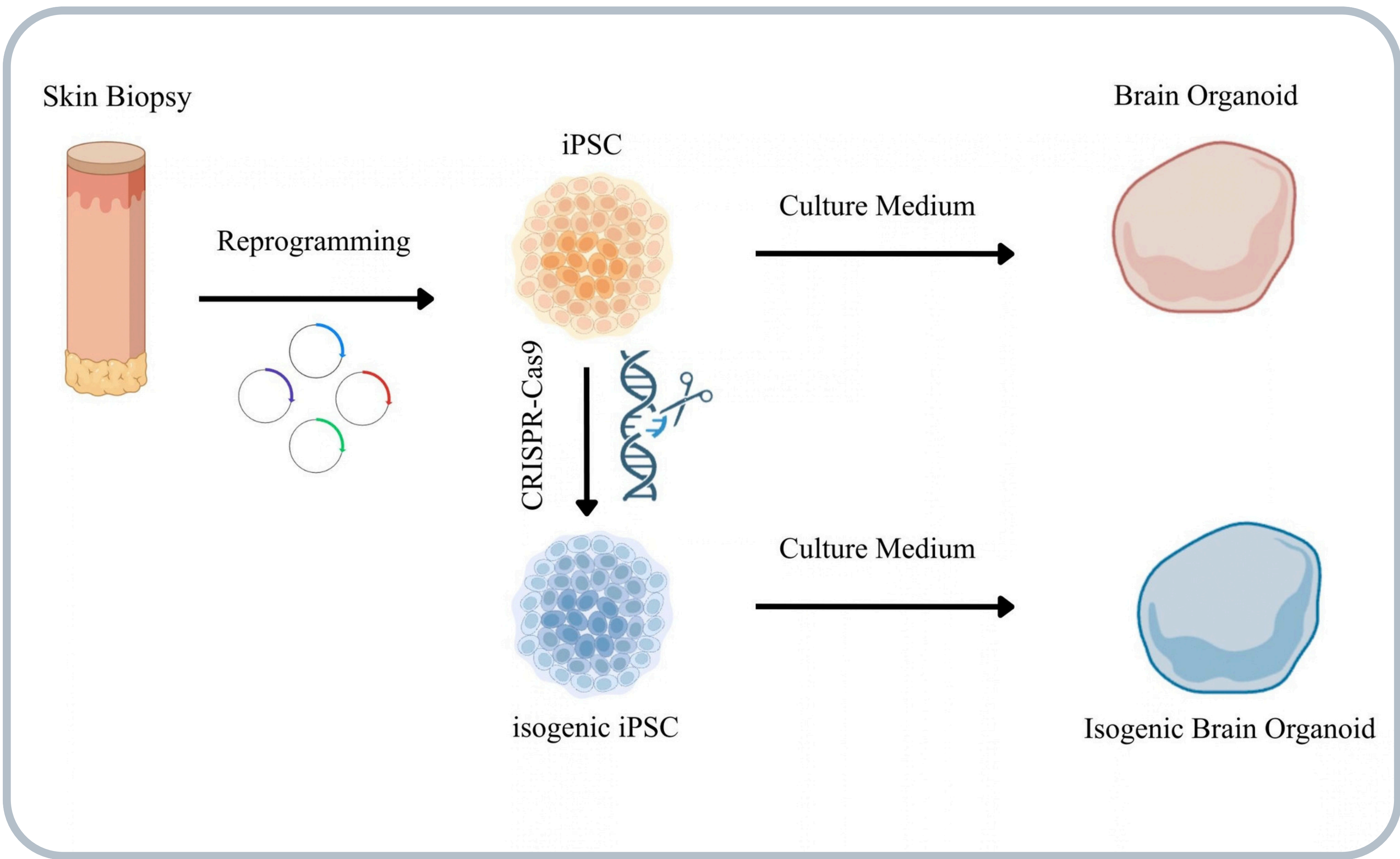
- Genetic control: Reduce genetic variation between samples.
- Mutation-specific insights: Isolate effects of specific AD-associated variants.
- Disease mechanisms: Reveal roles of ferroptosis, mitochondrial dysfunction, calcium dysregulation, and neuronal hyperexcitability.
- Drug screening: Evaluate disease phenotypes and potential treatments.

Discussion

- Advantage: Greater genetic control helps link variants to disease phenotypes.
- Limitation: CRISPR editing and organoid development introduce variability.
- Major limitation: Single variants cannot capture sporadic AD complexity.
- Implication: Isogenic organoids should complement, not replace, other models.

Conclusion

- Isogenic organoids provide greater genetic control for studying AD-associated variants.
- They reveal cellular and neuronal disease mechanisms and support drug screening.
- Technical and biological limitations remain.
- Best used alongside patient-derived models, animal studies, and clinical research.



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