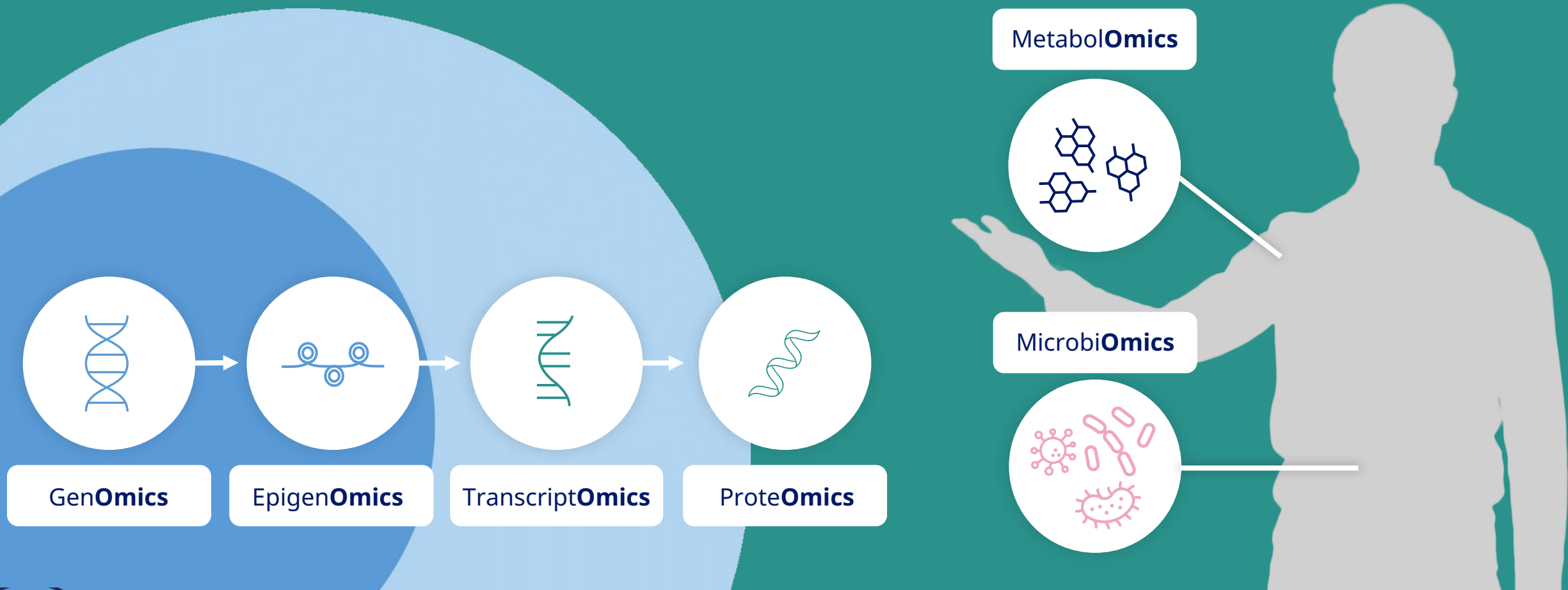# Alzheimer's disease
in the omics era

Alzheimer's disease
in **the omics era**

Using 'Omics' to identify, describe and quantify biomolecules and molecular processes

MetabolOmics

MicrobiOmics

GenOmics → **EpigenOmics** → **TranscriptOmics** → **ProteOmics**

1. Karczewski KJ and Snyder MP. *Nat Rev Genet* 2018;19:299–310.
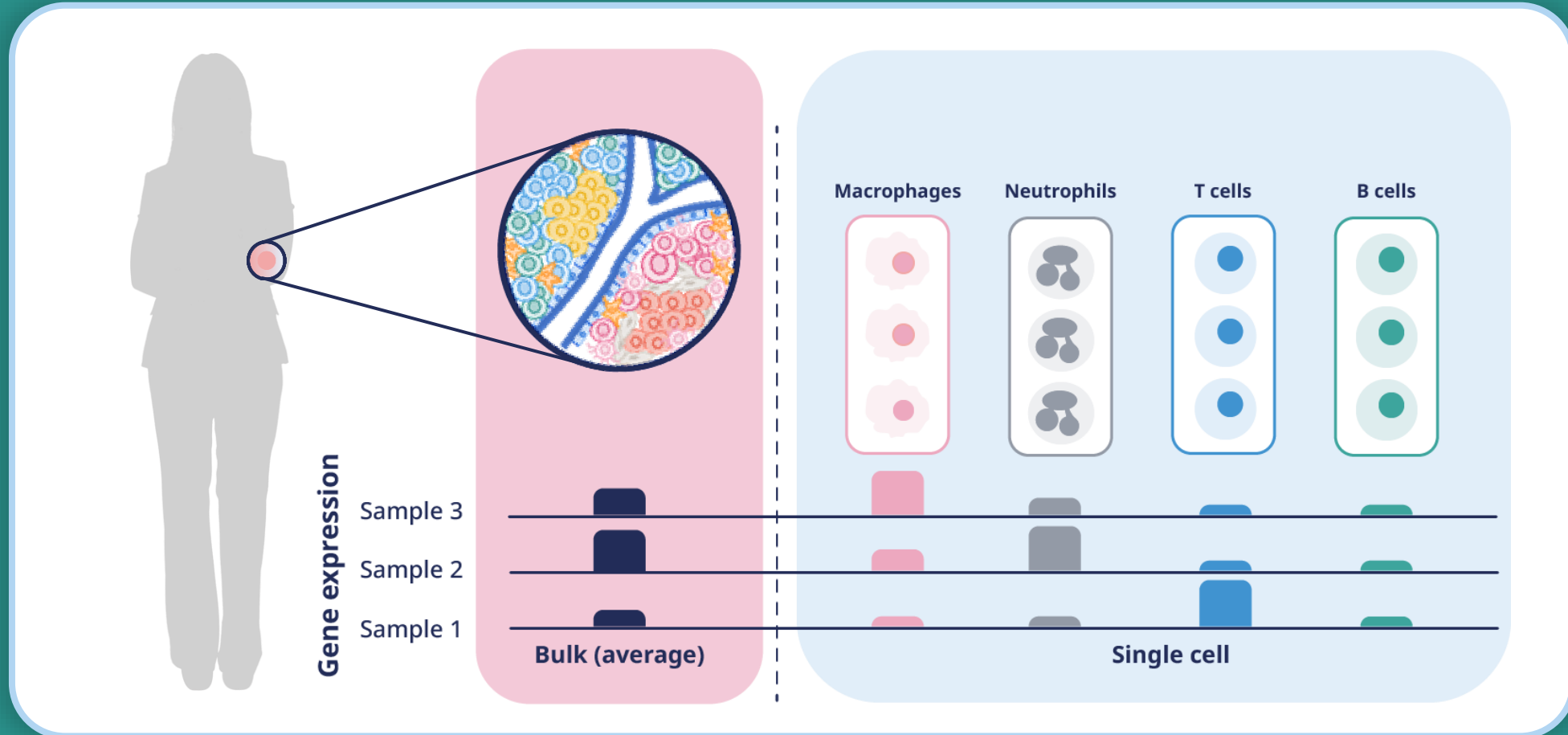
'Bulk' versus single-cell transcriptomics
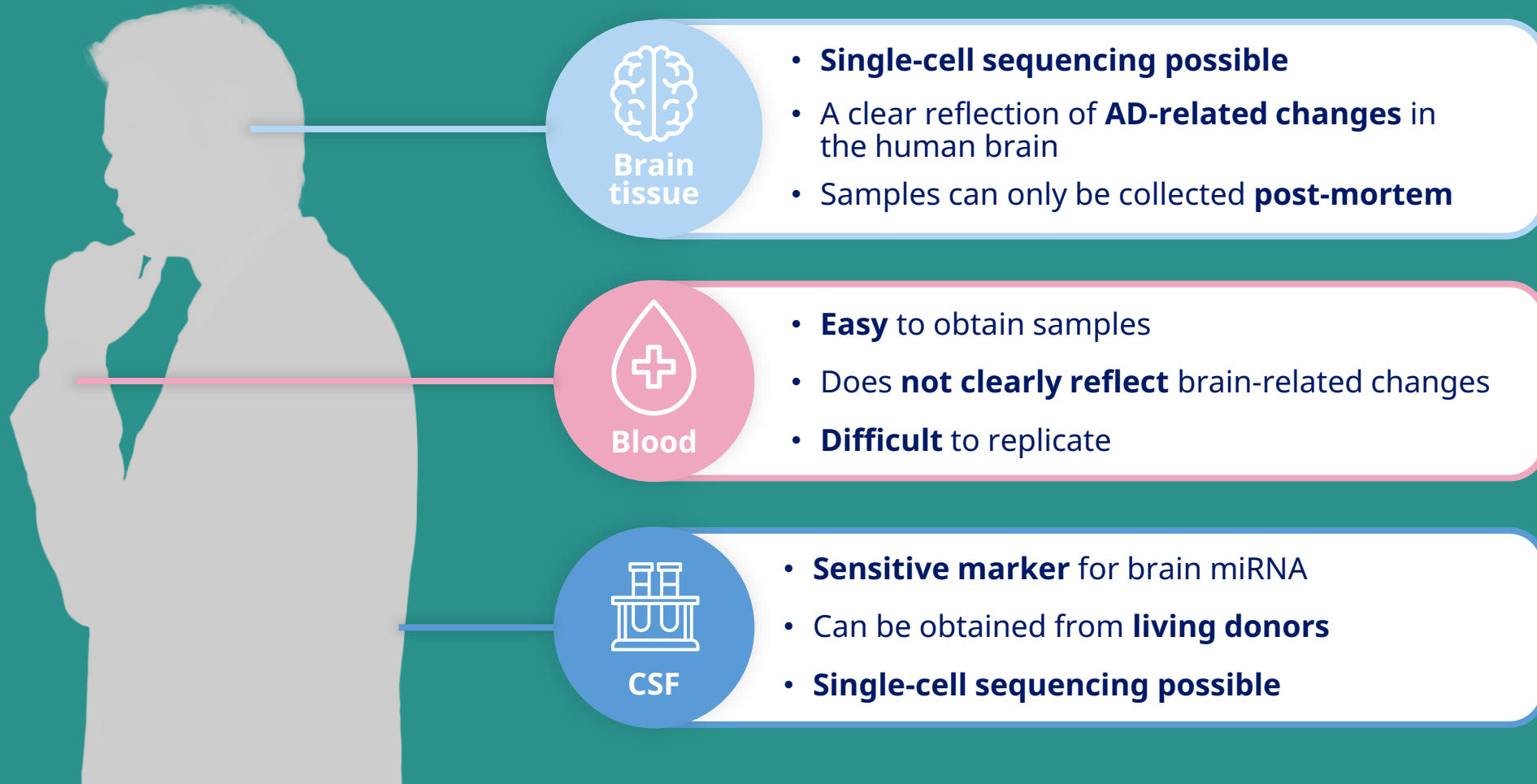

Figure adapted from Fan J et al. *Exp Mol Med* 2020;52:1452–65.

Transcriptomics sample types in Alzheimer's disease

Brain tissue
- **Single-cell sequencing possible**
- A clear reflection of **AD-related changes** in the human brain
- Samples can only be collected **post-mortem**

Blood
- **Easy** to obtain samples
- Does **not clearly reflect** brain-related changes
- **Difficult** to replicate

CSF
- **Sensitive marker** for brain miRNA
- Can be obtained from **living donors**
- **Single-cell sequencing possible**

'Omics' approaches have huge potential in drug development and disease understanding

Target identification and pathology understanding

Preclinical model selection

Mode of action understanding

Drug candidate selection

Biomarker discovery

Disease subtyping and patient stratification

Disease progression and monitoring

Single-cell atlas of the aged human prefrontal cortex across 427 individuals

427 ROSMAP study participants

Prefrontal cortex → Droplet-based snRNA-Seq → **2.3 million** Single-nucleus transcriptomes of the aged human brain
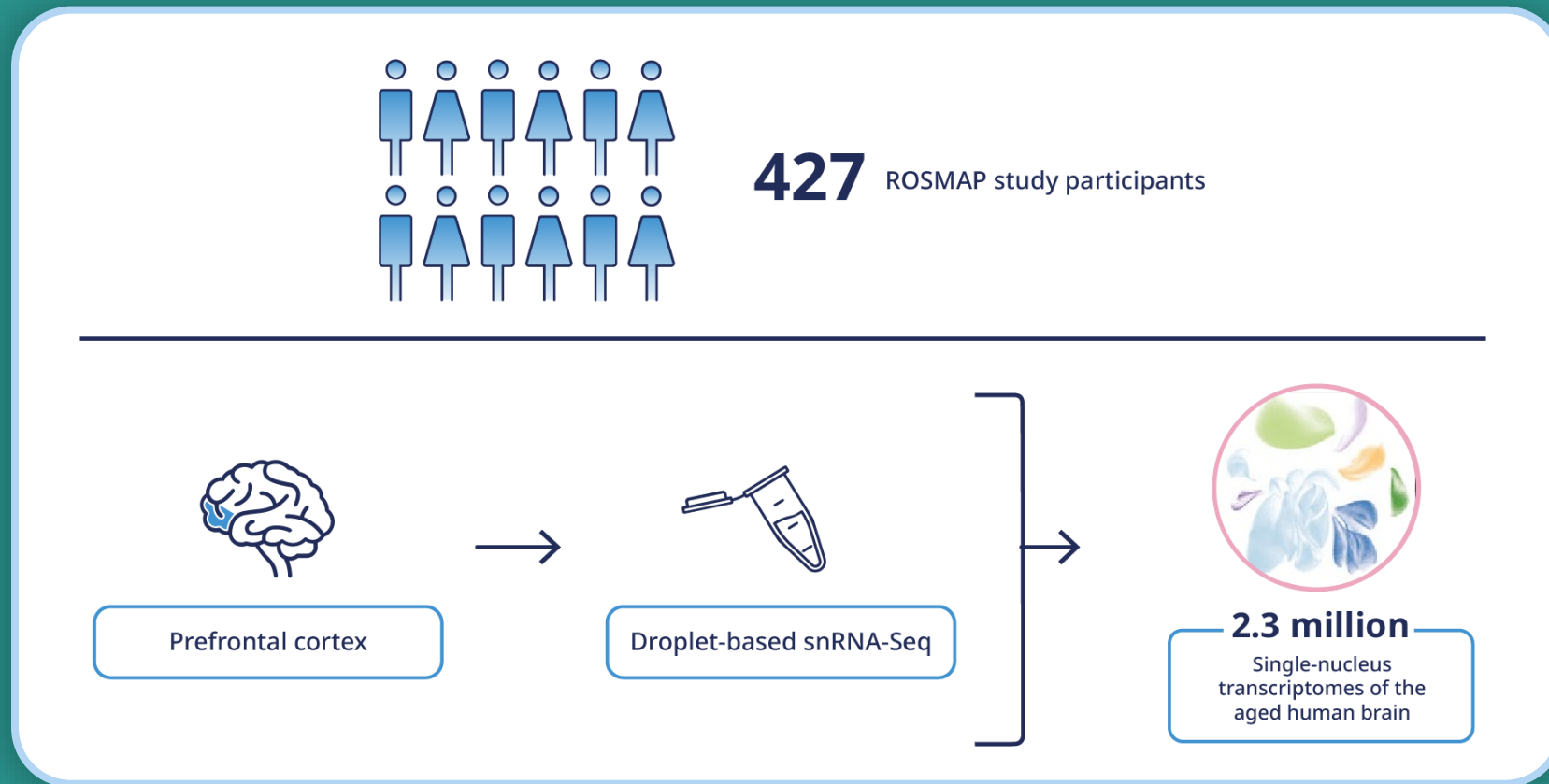
3 key learnings

1 "Omics" (transcriptomics, proteomics) can aid in identifying novel drug targets, gaining a better understanding of pathophysiology, assessing potential treatment effects, and discovering novel biomarkers.

2 In contrast to bulk omics, single-cell techniques (performed on either post-mortem brain tissue or CSF/blood samples) provide knowledge on which specific cells and pathways are being modified throughout the disease course or by a drug or clinical intervention.

3 Single-cell atlas of the human brain are unravelling genes and transcriptomic changes associated with cognitive decline as well as preserved cognitive function (resilience factors).

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References

Bagyinszky E et al. Int J Mol Sci 2020;21:3517

Fan J et al. Exp Mol Med 2020;52:1452–65

Karczewski KJ and Snyder MP. Nat Rev Genet 2018;19:299–310

Mathys H et al. Cell. 2023 Sep 28;186(20):4365-4385.e27

Van de Sande B et al. Nat Rev Drug Discov 2023;22:496–520