

Brain-on-a-chip technology to develop precision medicine for brain disorders

Prof. dr. Nael Nadif Kasri
Radboud UMC, Nijmegen



Image AI generated

Traditional drug development pipeline



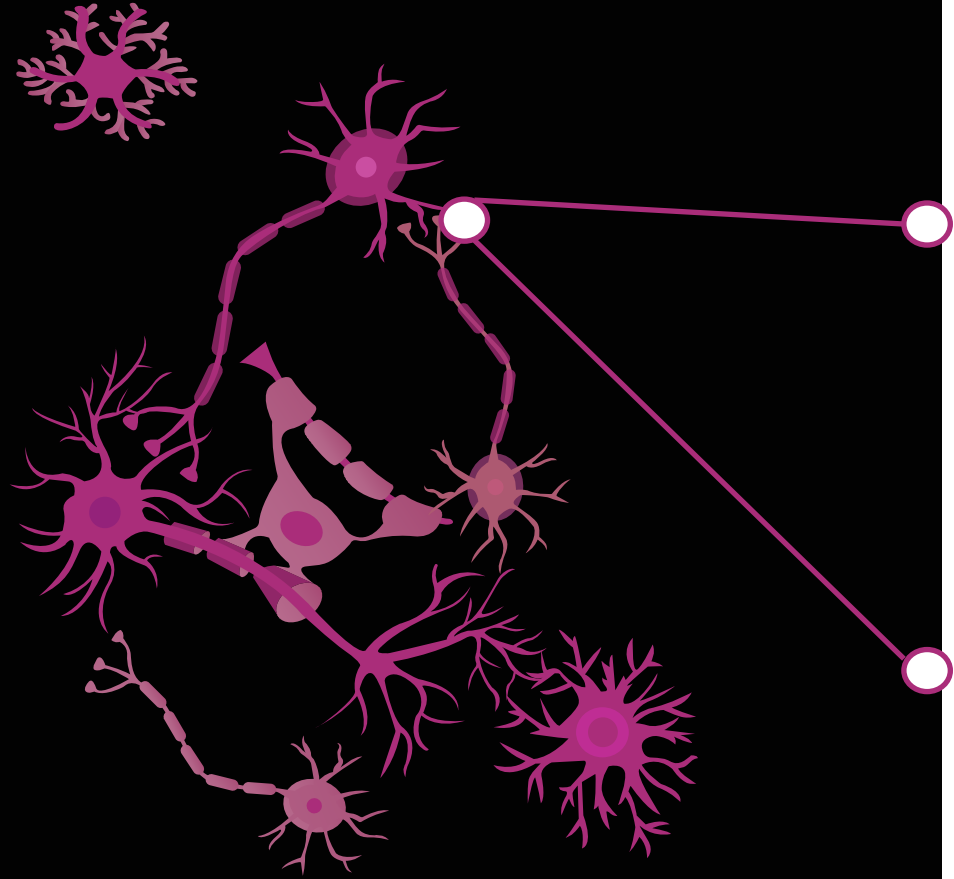
“The good physician treats the disease; the great physician treats the patient who has the disease” - William Osler 1849-1919

Father of Modern Medicine



NETWORK

- *86 billion neurons*
- *250,000 neurons per minute*

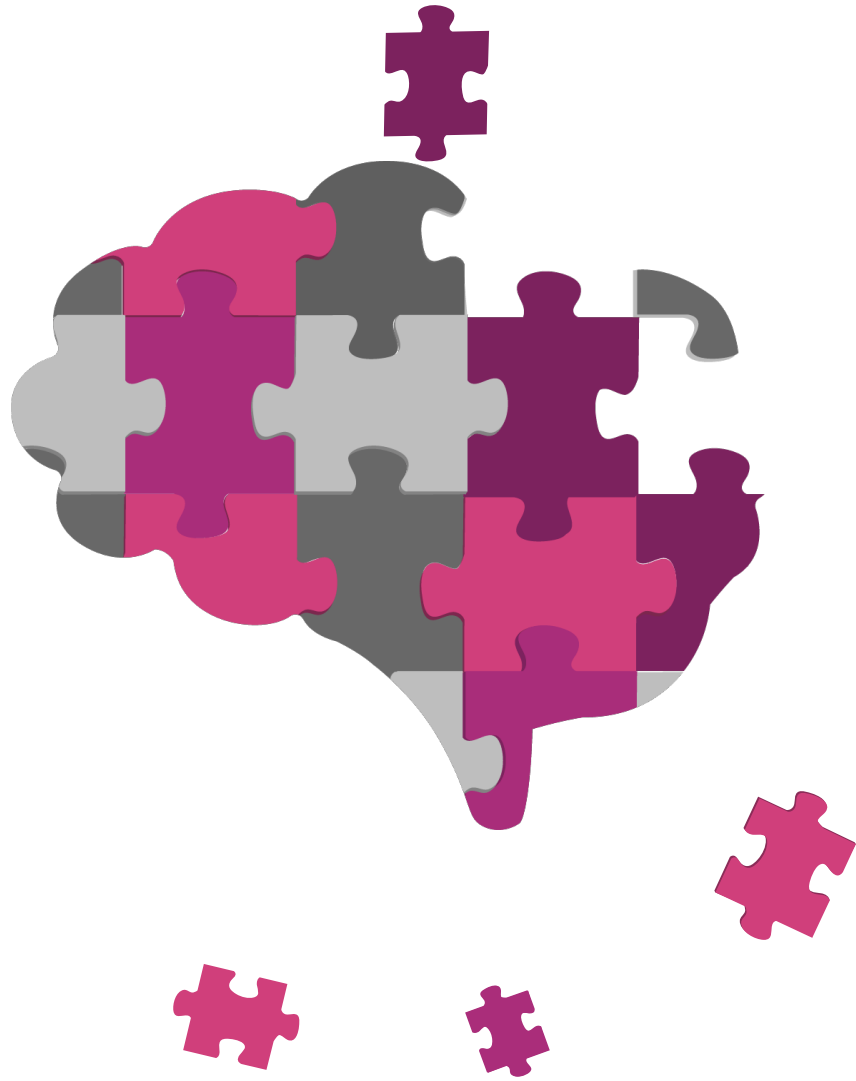




SYNAPSES







The human brain is complex and not accessible

Better understand the brain by assembling it ... in the lab


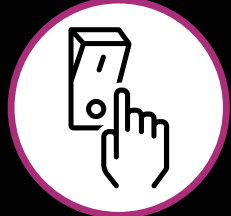









BRAIN ASSEMBLY INSTRUCTIONS  




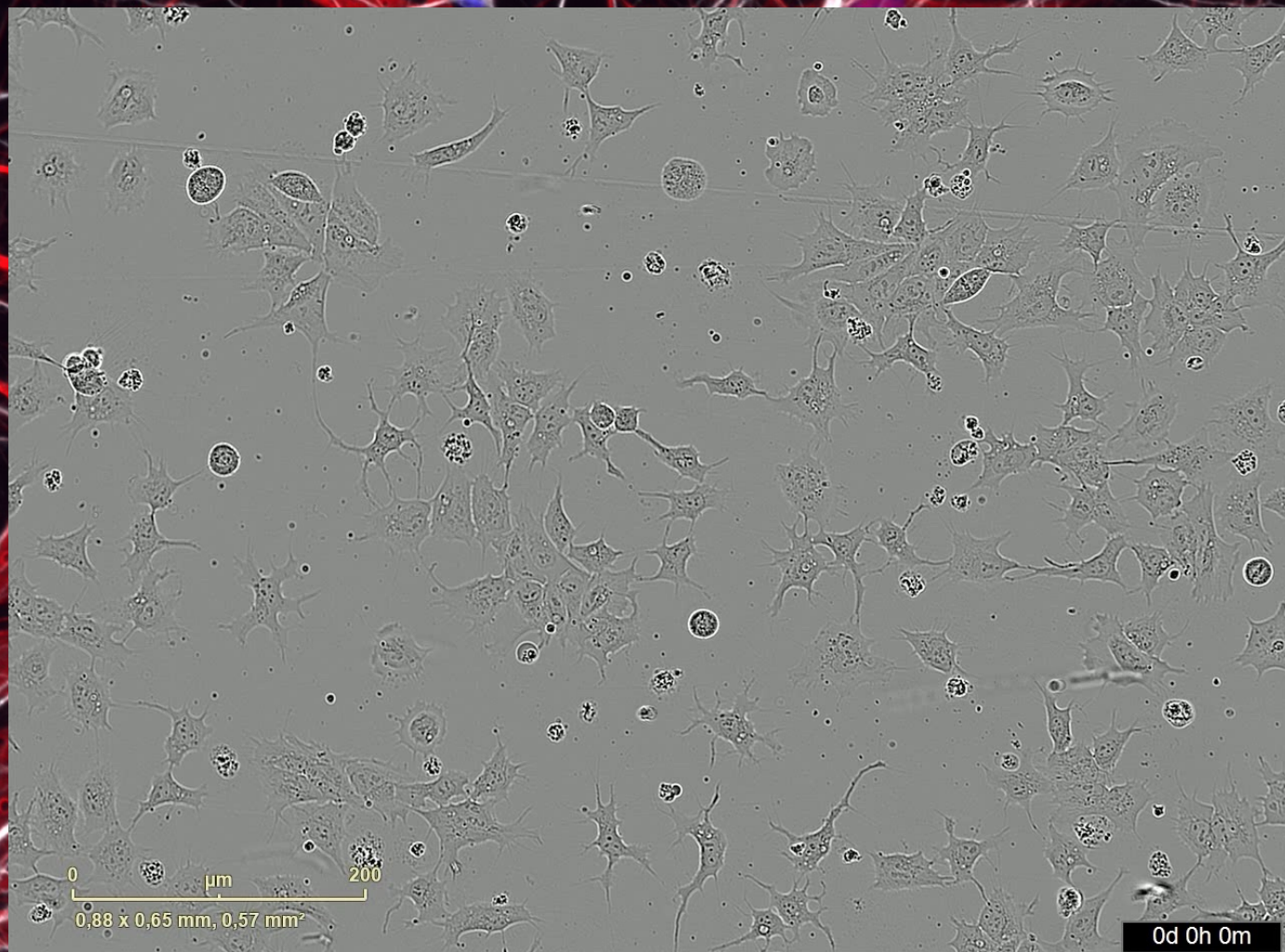
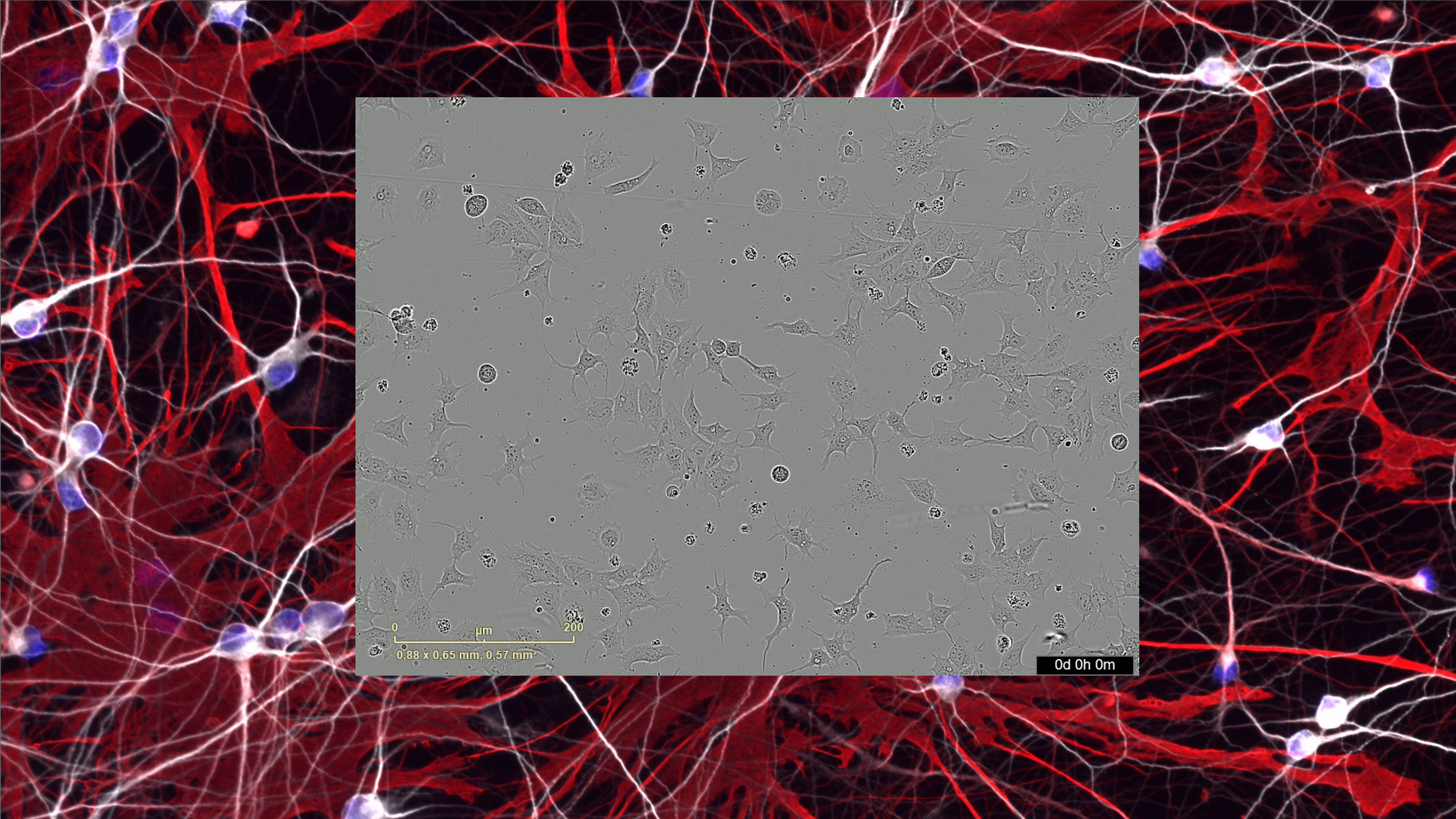
		
Brain	Nerves	Body
1x	1,000,000,000x	1x

Cellular time travelling: Stem cells

 Gene A	 Gene A	 Gene A
 Gene B	 Gene B	 Gene B
 Gene C	 Gene C	 Gene C

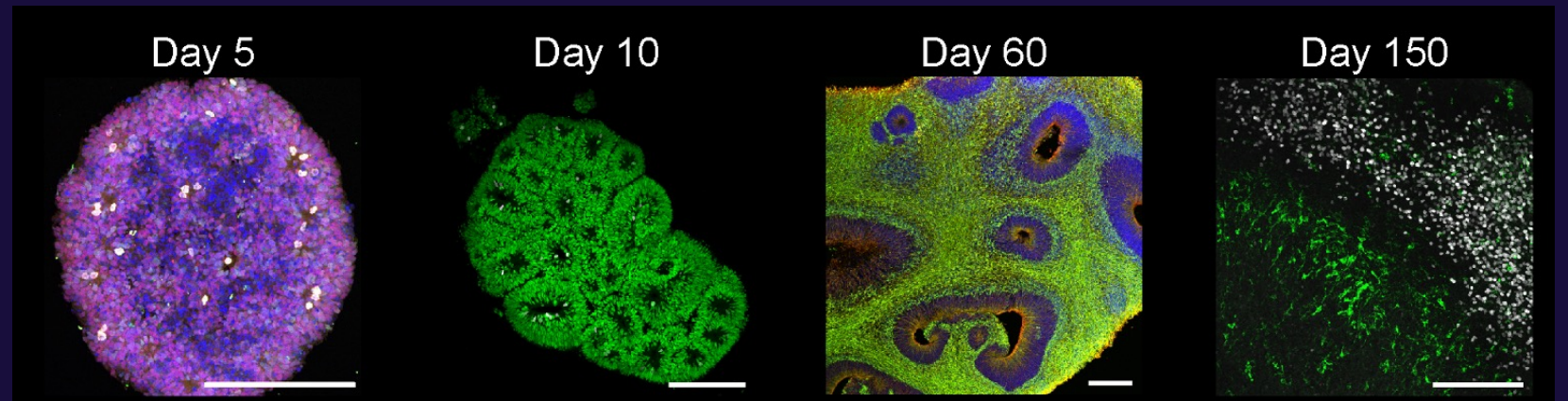
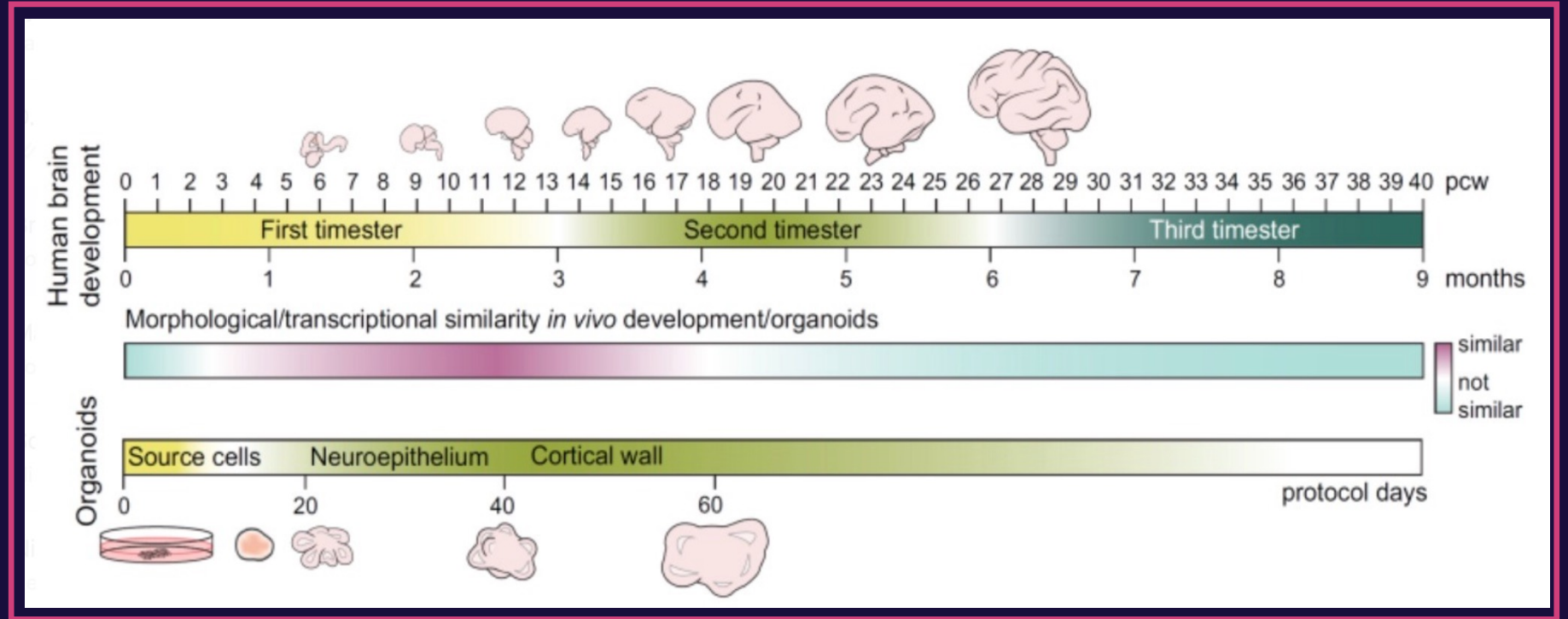
⋮

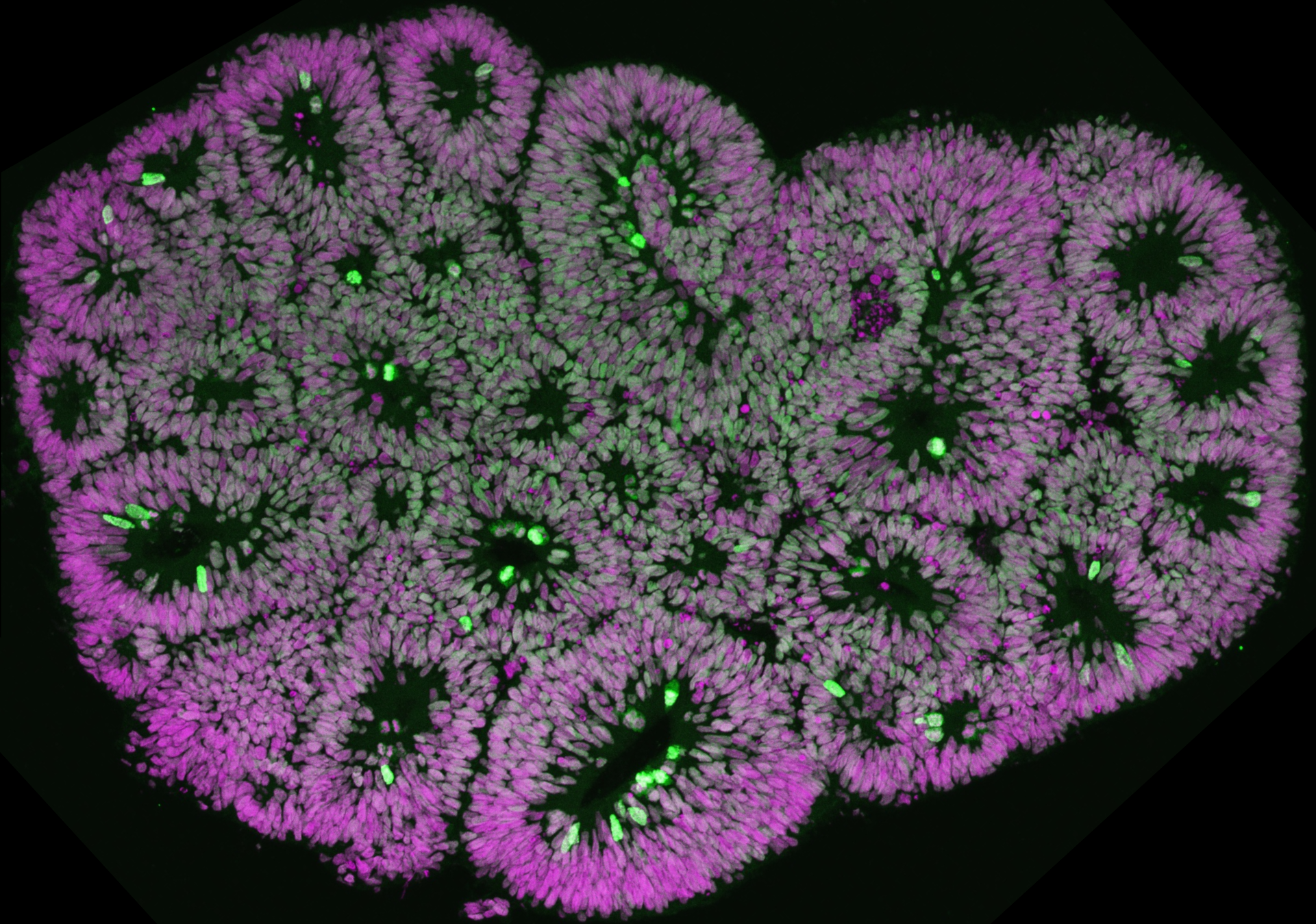


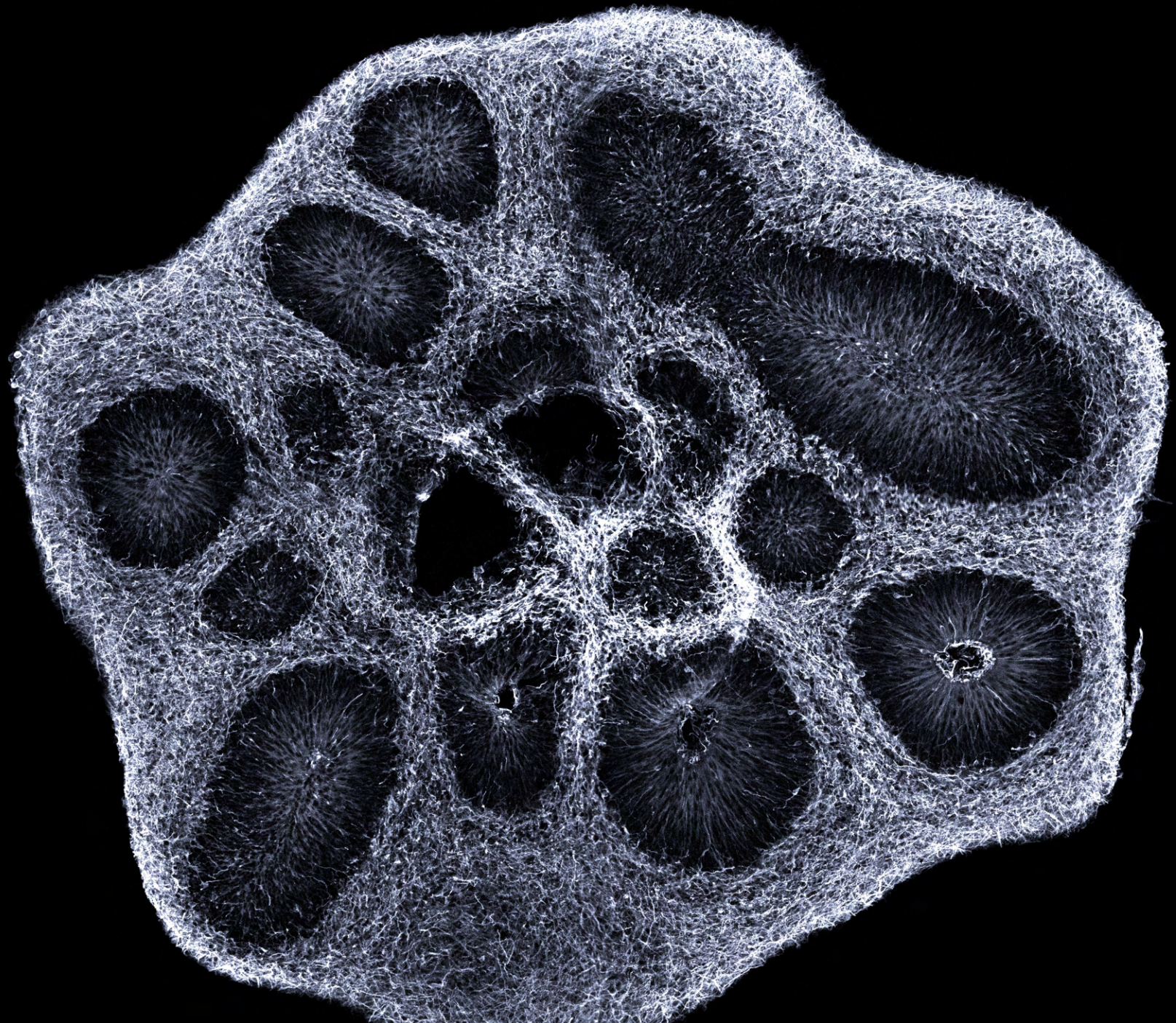




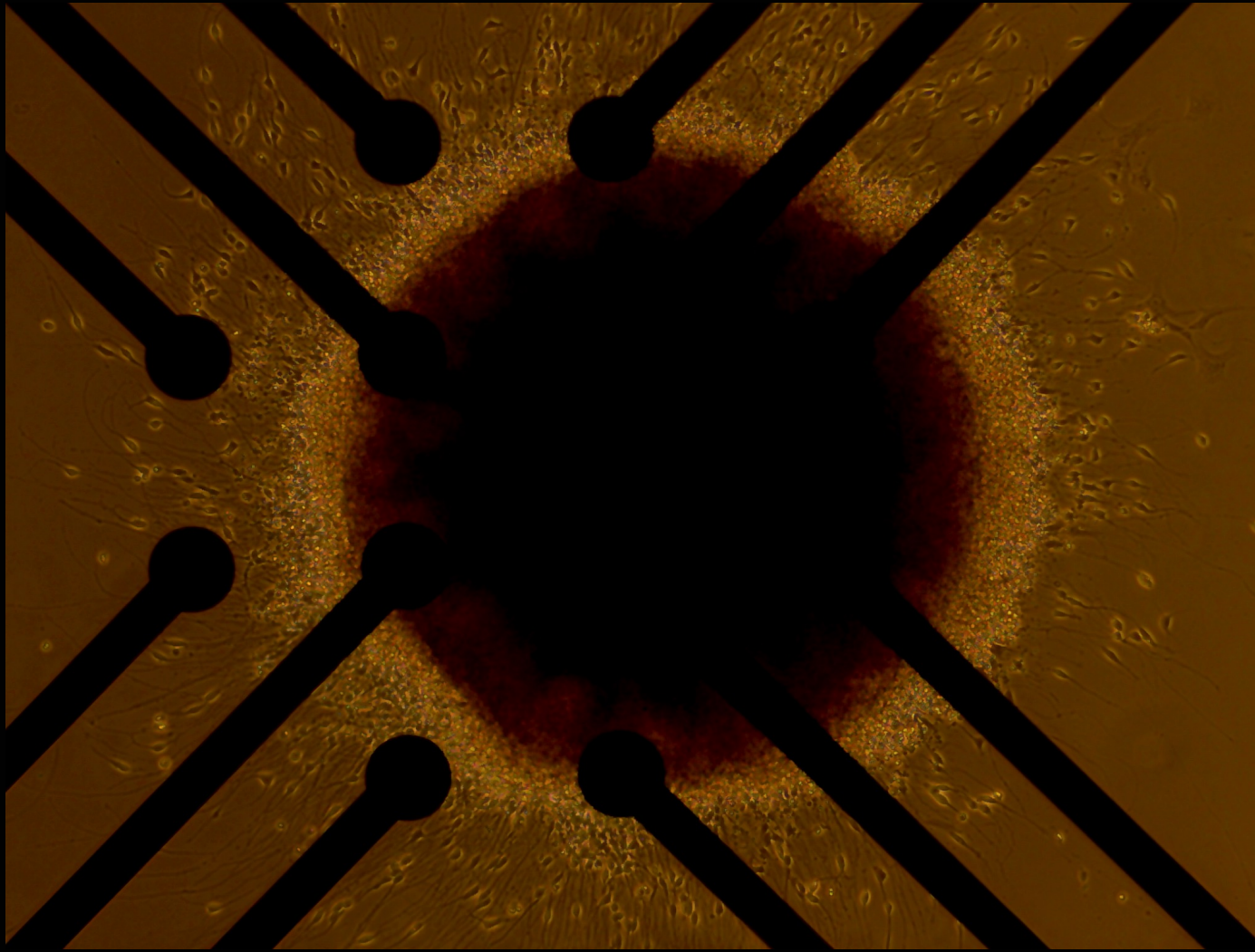
Brain organoids follow a developmental trajectory reminiscent of human brain development



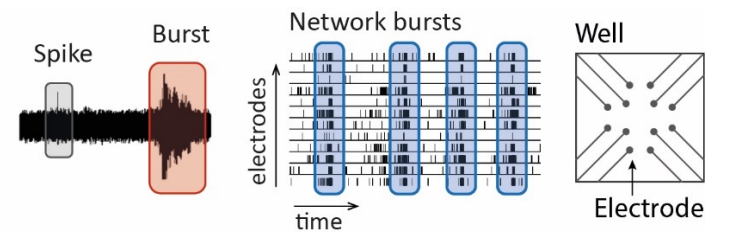
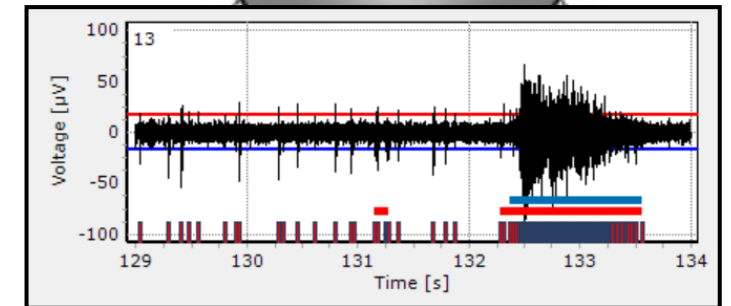
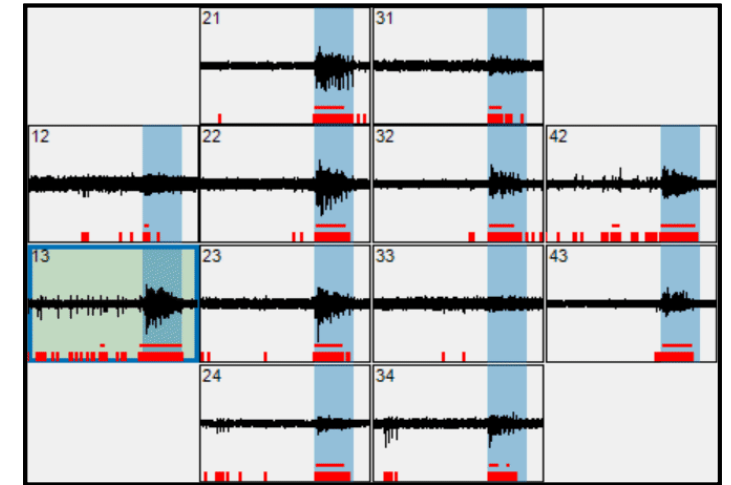




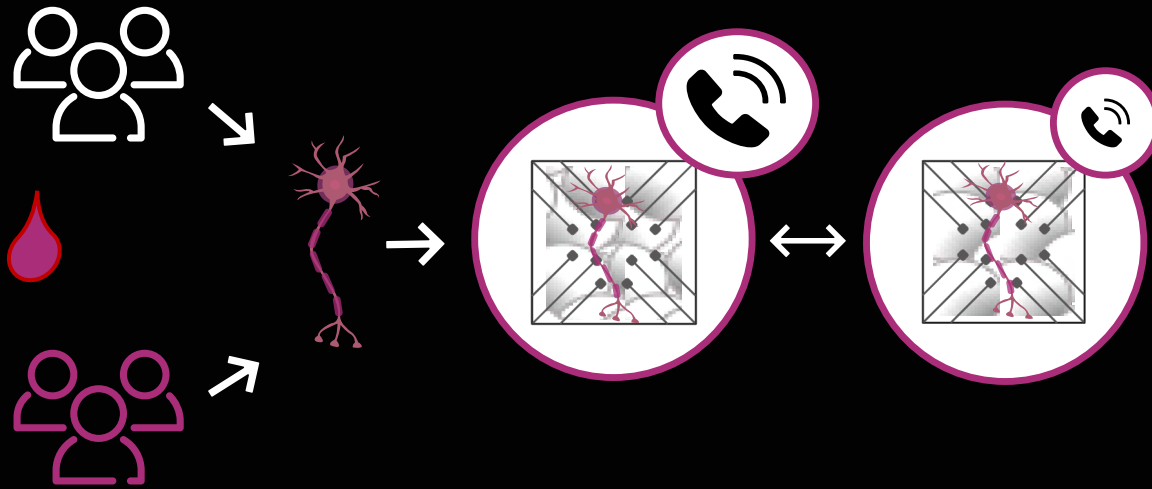
Cerebral organoids on a chip: Micro electrode Arrays



Micro-electrode array (MEA) system

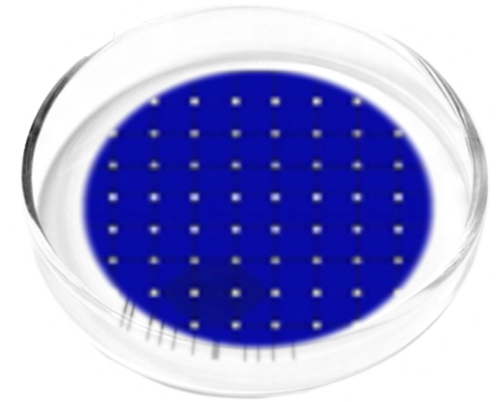


BRAIN-on-a-CHIP TECHNOLOGY



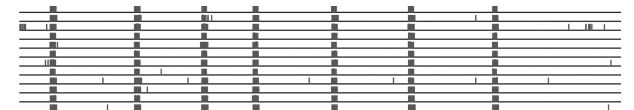
When?

How often?

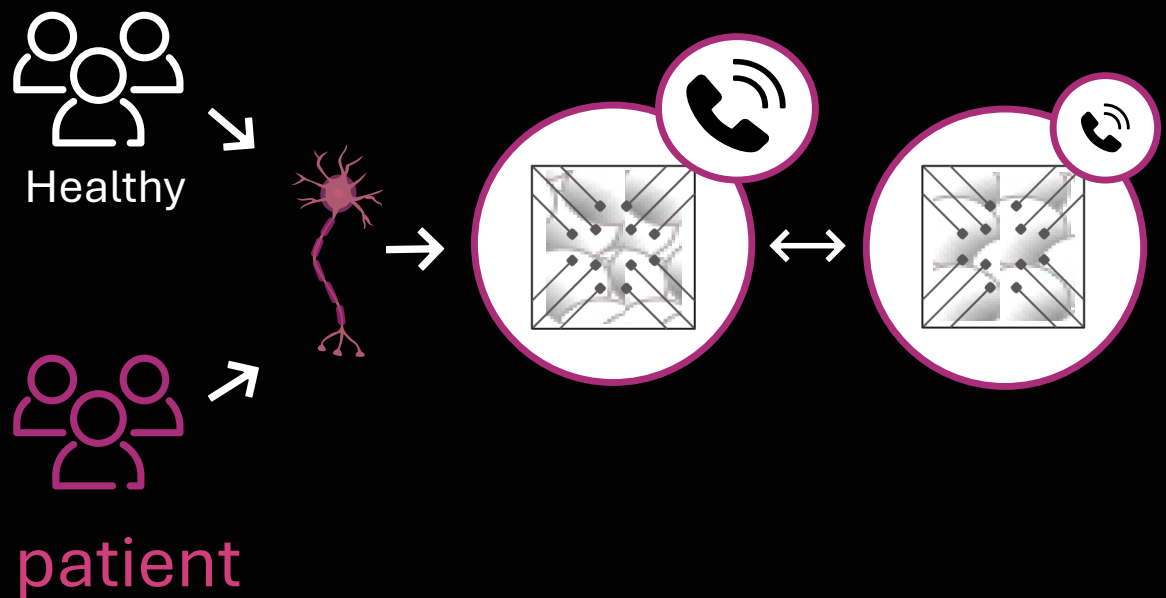


With whom?

How loud?

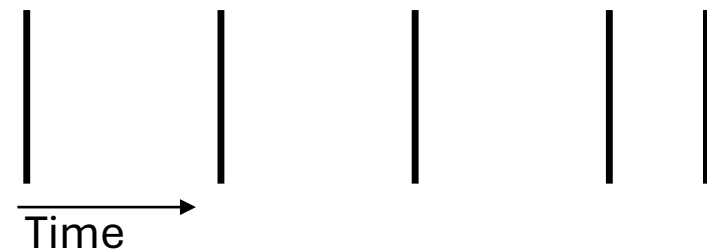


BRAIN-on-a-CHIP TECHNOLOGY

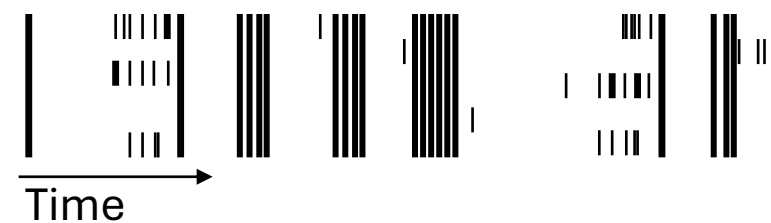


Healthy

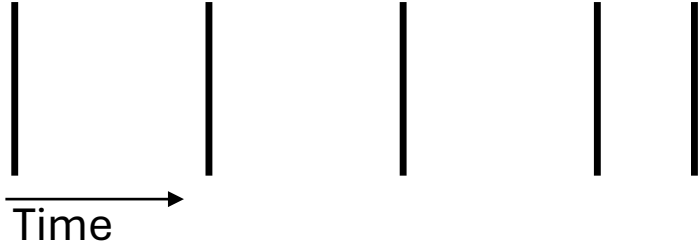
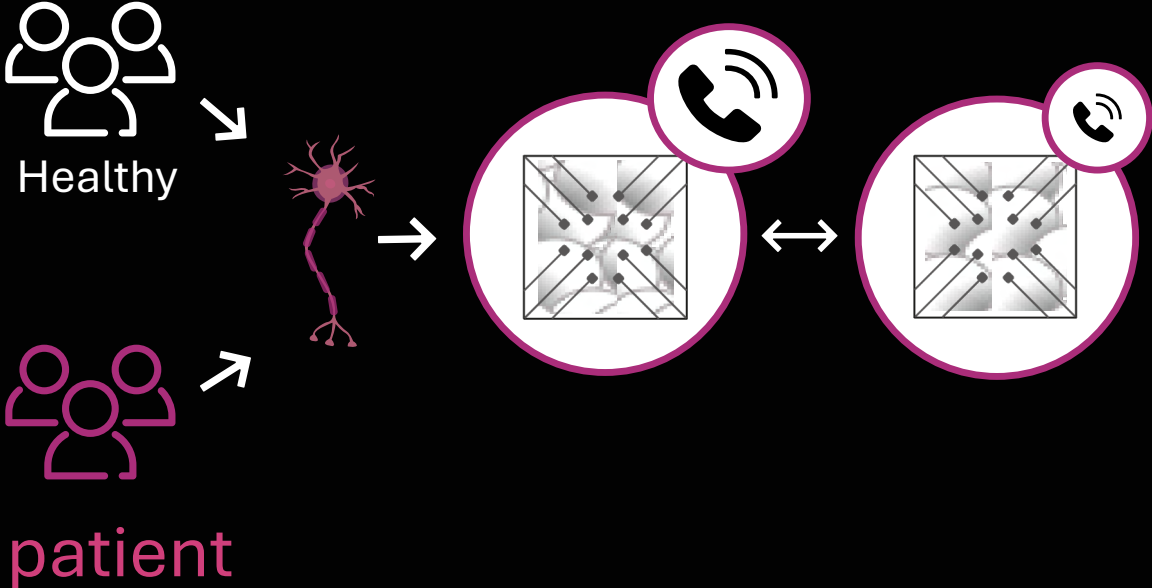
patient



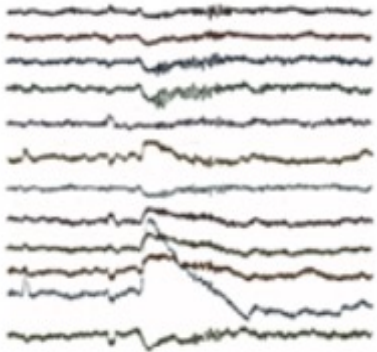
Network fingerprint



BRAIN-on-a-CHIP TECHNOLOGY



EEG



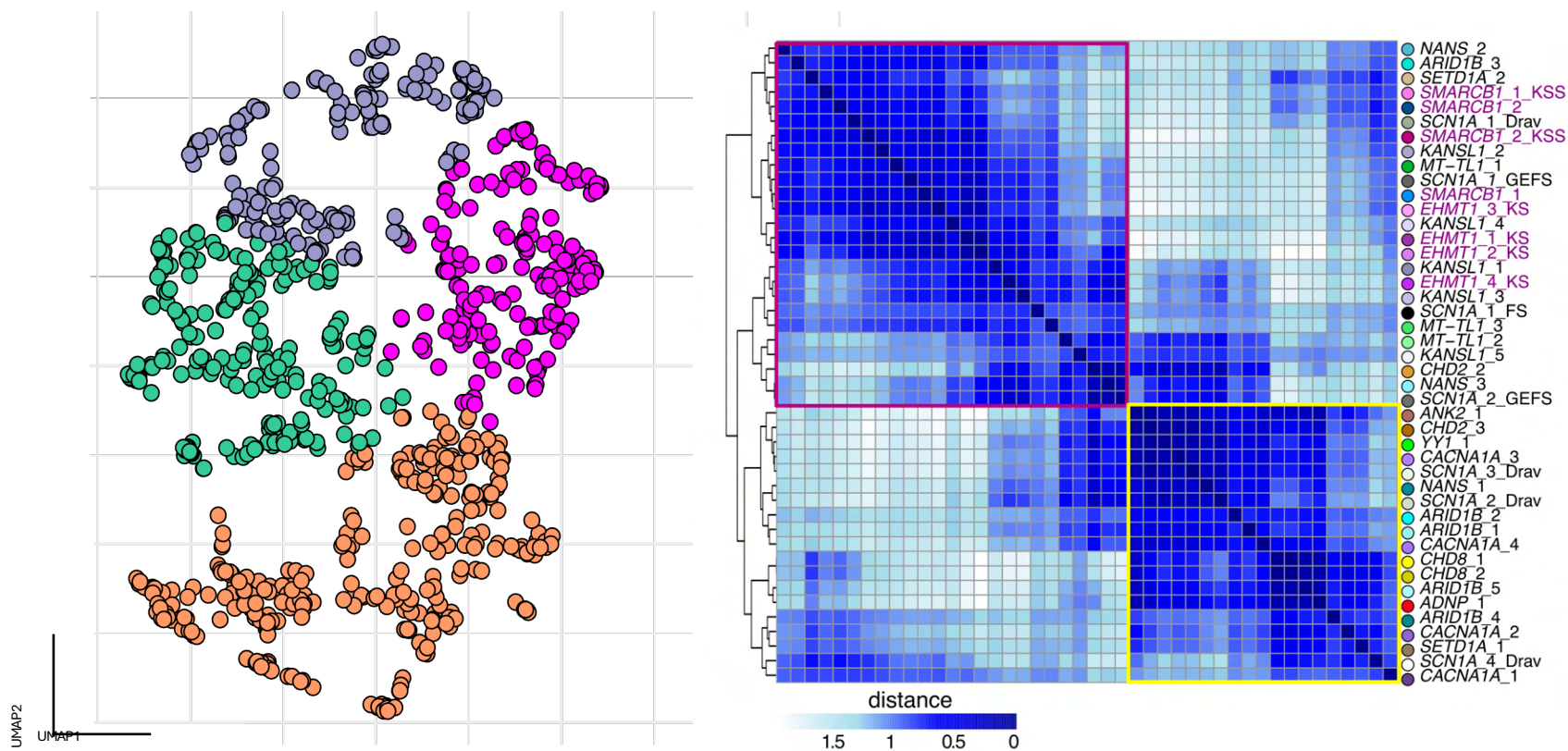
Research questions



- What is the patient/disease fingerprint?
- Can we predict the effect of medication, for example anti-seizure medication?
- Can we use brain-on-a-chip models to test genetic therapies?

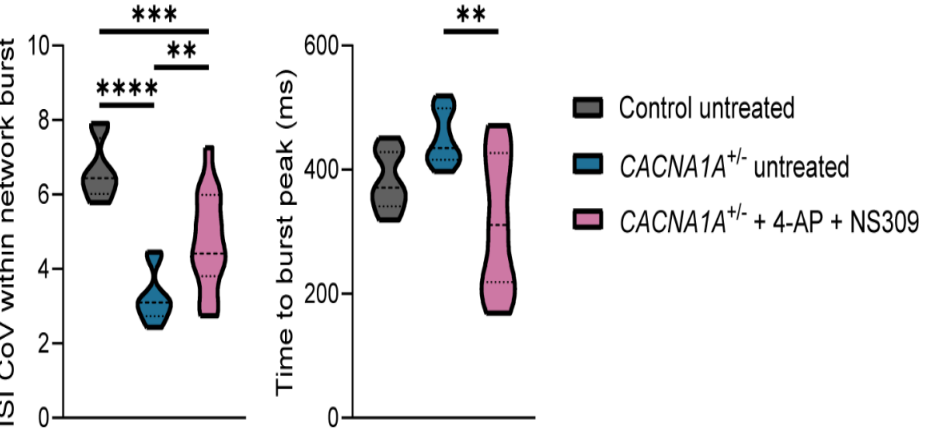
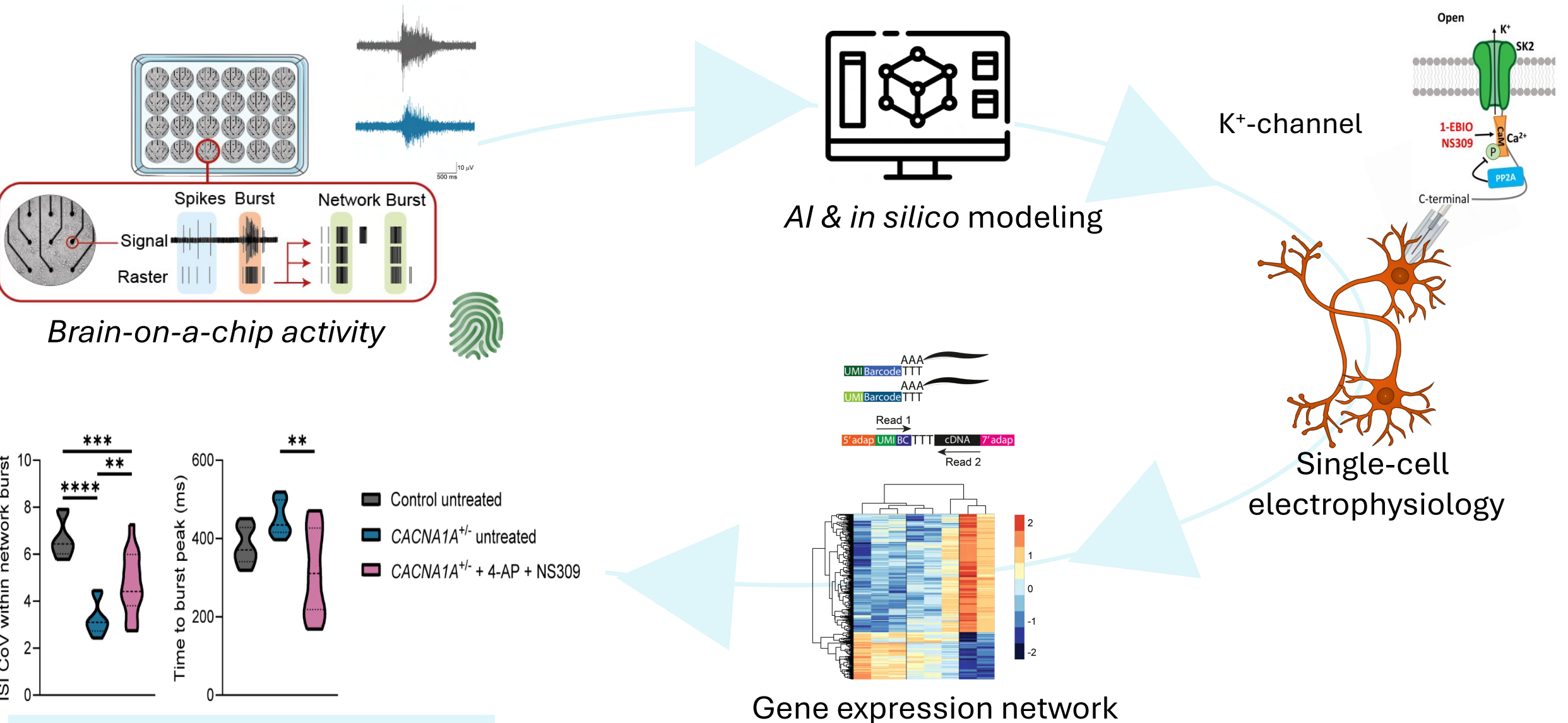


Patient-specific network signatures during development



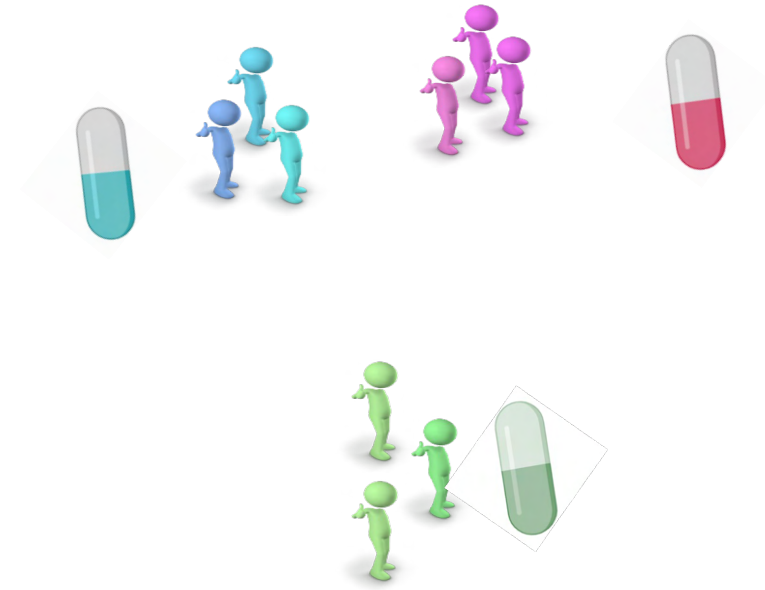
16 disorders and 45 patients

Example: beneficial effect of combinatorial drug treatment in ataxia/epilepsy disorder

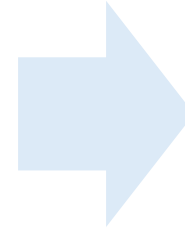
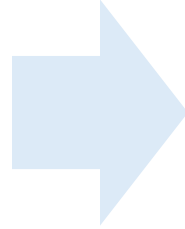


Combinatorial use of 4-AP and NS309 rescues network phenotypes

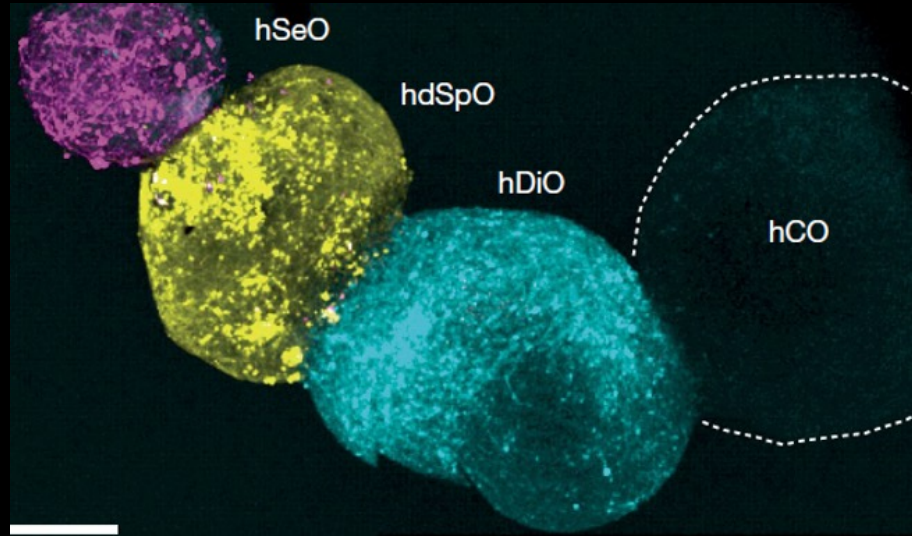
Precision medicine for brain disorders



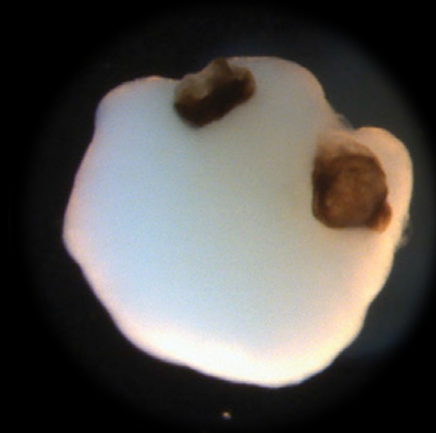
Precision medicine for brain disorders



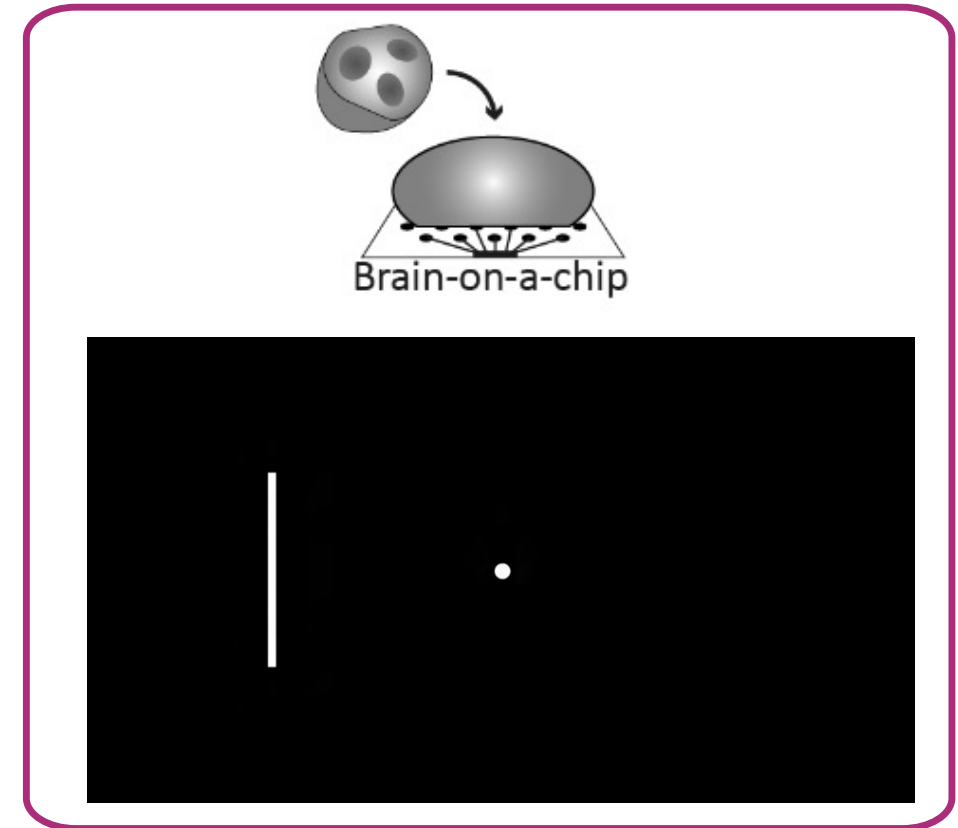
Advanced complex brain models



Pain circuitry



Organoid intelligence



Organs-on-a-chip

