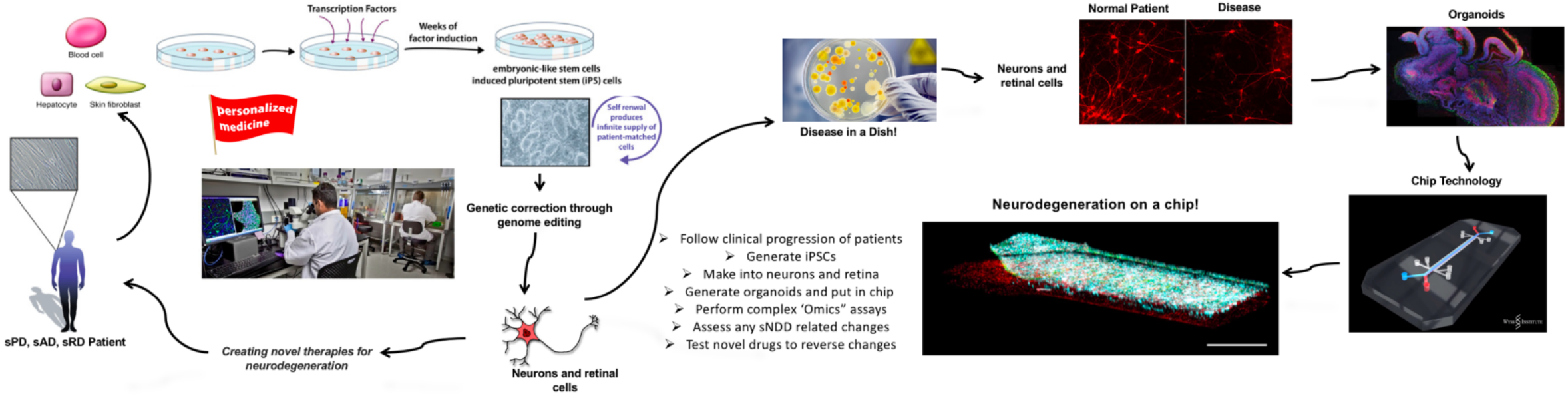
Session 6.

Taking the Regenerative ND Candidate to the Clinic



FTD ADRD: Advance FTD clinical trial design - Needs and Barriers

- **There is need to facilitate and manage new and ongoing FTD prevention studies and clinical trials.**

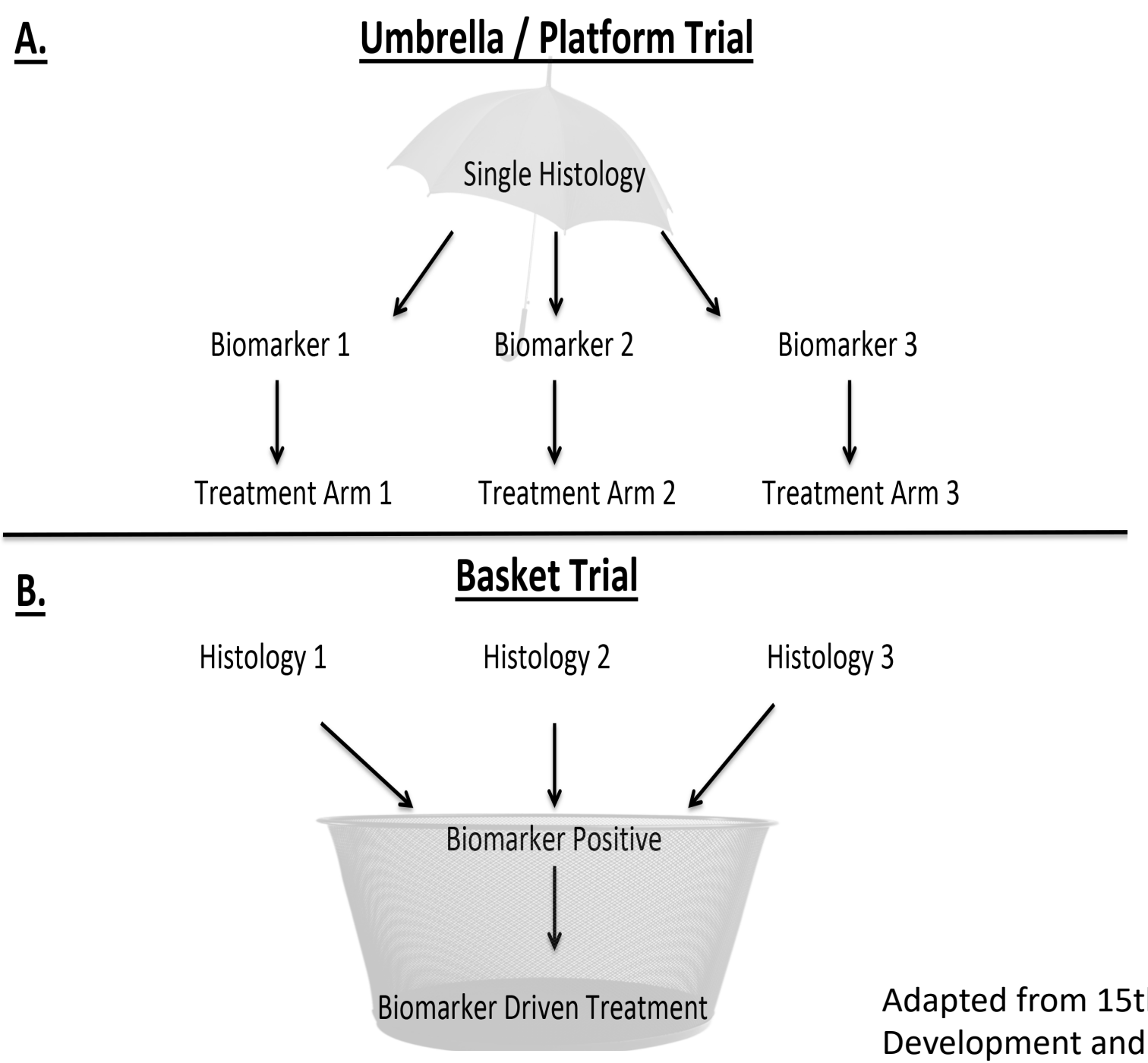
- **The rarity of FTD patients and asymptomatic mutation carriers is a major barrier to testing new therapies.**

- **Moreover, in some populations, the initiation of a clinical trial will prevent further collection of natural history data.**

FTD ADRD: Advance FTD clinical trial design and execute studies - Recommendations

- **Expand support for ascertaining both familial and sporadic cohorts**
- **Collect clinical, genetic, and biomarker data using a centralized database/coordinating center.**
- **New statistical methods to build more powerful endpoints**
- **Master protocols should be developed to enable rapid implementation of emerging therapeutic approaches.**

- **Conduct community outreach efforts and build tools (such as online registries) to engage underserved, minority and remote populations for inclusion in natural history and clinical trials.**



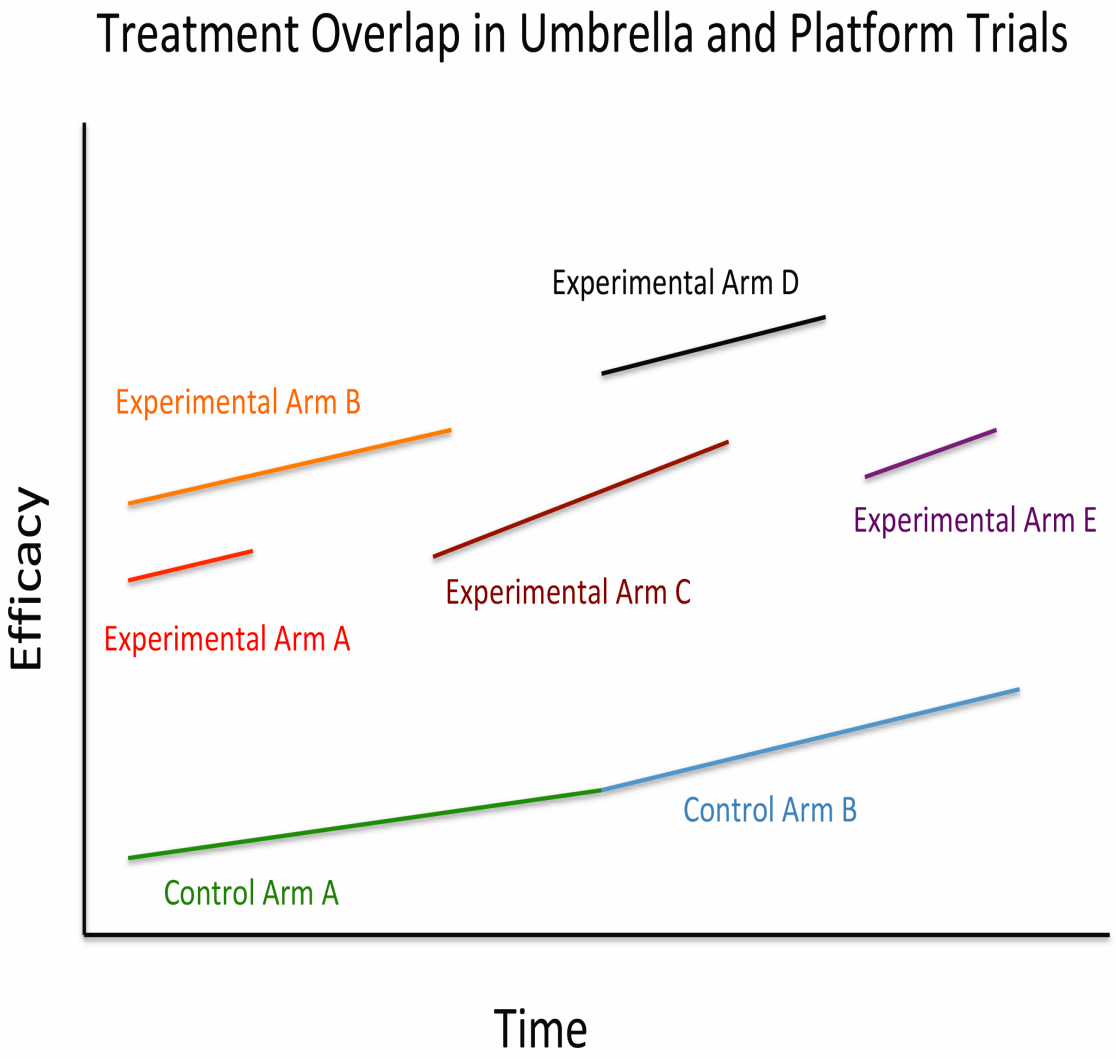
Umbrella/Platform Studies:

- one neurodegenerative disorders, multiple genetic changes/phenotypic changes
- each patient is assigned to a personalized treatment arm based on their biologic make-up

Basket Studies:

- multiple disorders that share common pathways for some of their patients (rare subpopulations)
- all the patients with the same abnormal pathway will be treated with the same treatment irrespective of the pathology

Adapted from 15th Annual 2018 Accelerating Anticancer Agent Development and Validation (AAADV) and Cecchini, M at all, CCR, 2019



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Umbrella/Platform Studies:

Multiple challenges

- adding and removing treatment arms
- maintaining the appropriate simultaneous controls
- each patient is assigned to a personalized treatment arm based on their biologic make-up

Advantages

- multiple treatment arms allow the collaboration between multiple sponsors
- allow to minimize the number of controls
- requires synchronized regulatory submissions

The Clinical Integration Challenge

- **Novel study designs based on avatar models**
- **Studies of one (values)?**
- **Relevant Patient-Oriented Outcomes**
- **Relevant Economic and Societal Outcomes (cost of cure, delay of disability, work reintegration, etc)**

A Consortium of Consortia

- **Pros and Cons**
- **Avatar-linked registries (need for big data)**
- **Natural history and real life evidence (patient and society)**
- **Coming together for studies that require power in numbers (umbrella and basket studies)**