Biomarkers in Early Management of Concussion

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Concussion Essentials

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Near Miss Funding Clinical Sciences Theme

Case Study

- Male HS-aged student, sustained a concussion wrestling with friends at school
- Physically smaller than his peers, picked up and slung into a rubbish bin (accidental)
- Possible brief LOC, taken to RCH by ambulance
- Presented to the ED same day of injury
  - Headache
  - Blurred vision
  - Dizziness
  - Nausea
  - Photophobia

Case Study

- Seen approximately 1 month post-injury
- Experiencing:
  - Headaches
  - Fatigue
  - Concentration difficulties
  - Labile mood
  - Easily overwhelmed in busy environments
  - Disrupted sleep (ruminating)
- Attending school infrequently, when attending he is often symptomatic and asks to go home
- Mother forced to take time off work to look after him, quite concerned

4 million children

globally each year[1]

1 in 5 children

will experience a concussion by the time they are 16 years-old[2]

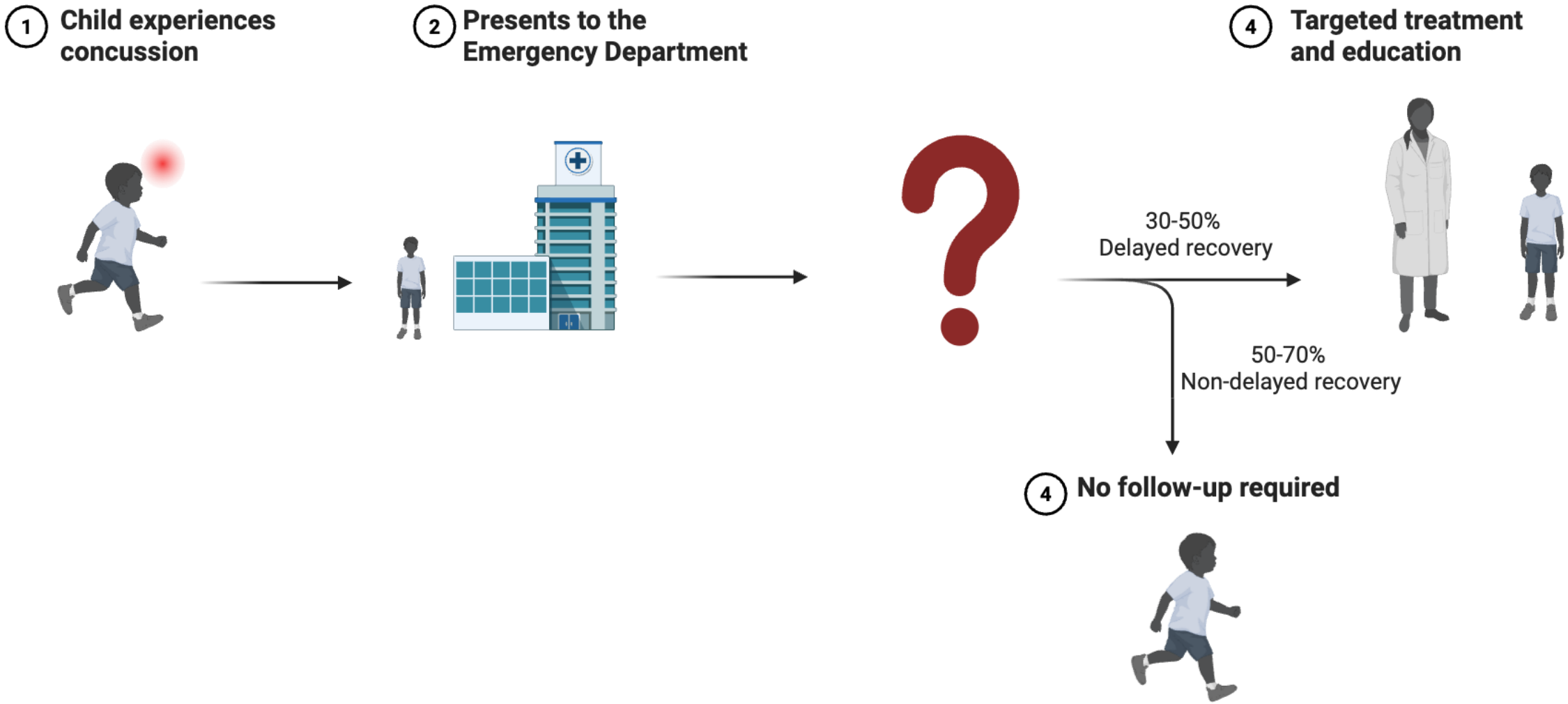
30-5  %

will experience **delayed recovery,** where

they will continue to have symptoms more than two weeks after their injury

e.g. headaches, fatigue, neck pain, difficulty concentrating, anxiety or depression[3]

[1]McCrea et al. 2004, Clinical Journal of Sports Medicine
[2]Anderson et al. 2020, Journal of Neurotrauma
[3]Mannix et al. 2019 Ann Emerg Med



[1]Rausa et al. 2025, Neuropsychological Rehabilitation

How do we predict delayed recovery from concussion?

Clinical risk factors

e.g. female sex, history of migraines, history of anxiety or depression, learning difficulties[1, 2]

Clinical assessment

e.g. Glasgow Coma Scale (GCS), Sports Concussion Assessment Tool (SCAT), Post-Concussion Symptoms Inventory (PCSI)[3, 4], 5P clinical prediction rule[7]

Neuroimaging

e.g. CT[5, 6]

[1]Zemek et al. 2013, JAMA Paediatrics
[2]Takagi et al. 2018, BMJ Open
[3]Yeates et al. 2022 ,BJSM
[4]Bressan et al. 2020, Journal of Paediatrics and Child Health
[5]Shapiro et al. 2019 J Neurotrauma
[6]Shukla et al. 2021 NeuroImage: Clinical
[7]Zemek et al. 2013 BMJ Open

How do we predict delayed recovery from concussion?

Vision

Gait & movement

Neuroimaging

Proteomic blood markers

How do we predict delayed recovery from concussion?

Vision

Gait & movement

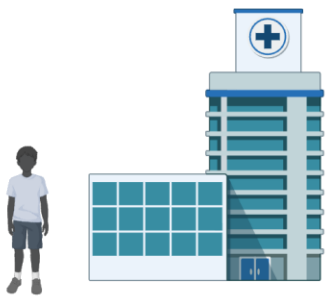
Neuroimaging

Proteomic blood markers

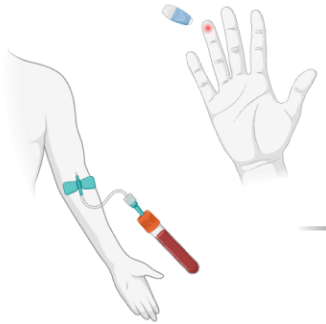
Cheap, convenient, not user dependent (objective)

1 **Child experiences concussion**

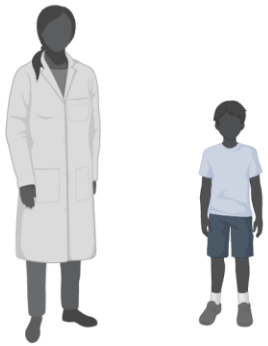
2 **Presents to the Emergency Department**



3 **Blood test to determine risk of delayed recovery**



30-50%
Delayed recovery



50-70%
Non-delayed recovery

4 **No follow-up required**

4 **Targeted treatment and education**

1 Blood biomarkers of secondary outcomes following concussion: A systematic review

SYSTEMATIC REVIEW article

Front. Neurol., 28 February 2023

Sec. Neurotrauma

Volume 14 - 2023 | https://doi.org/10.3389/fneur.2023.989974

Blood biomarkers of secondary outcomes following concussion: A systematic review

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Aims

Summarise state of knowledge on blood biomarkers of secondary outcomes following concussion

Analyse their potential as clinical tools for personalised treatment

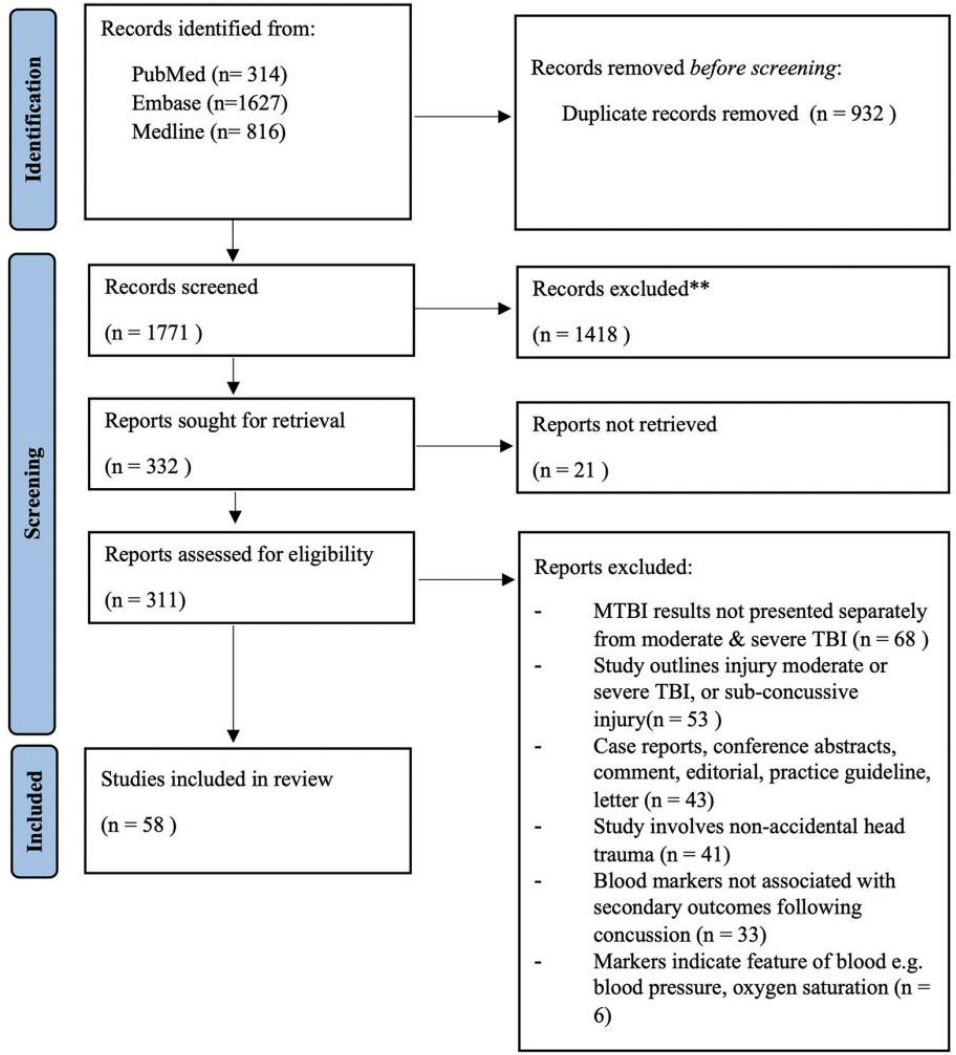
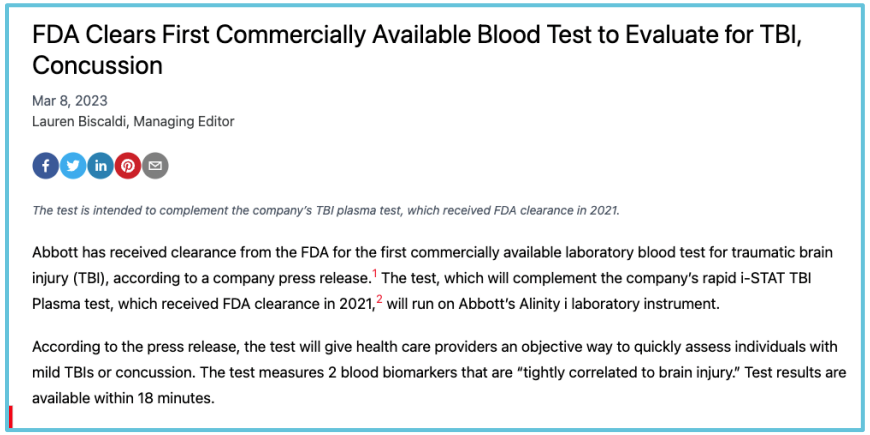


FIGURE 1
Summary of study selection process following PRISMA guidelines.

Key Findings & Recommendations

- Paediatric cohorts (n=10, 17%)
- Different definitions of concussion (n=11)
- Targeted analysis tools (n=41, 70%) - same markers investigated across numerous studies – no success



FDA Clears First Commercially Available Blood Test to Evaluate for TBI, Concussion

Mar 8, 2023
Lauren Biscaldi, Managing Editor

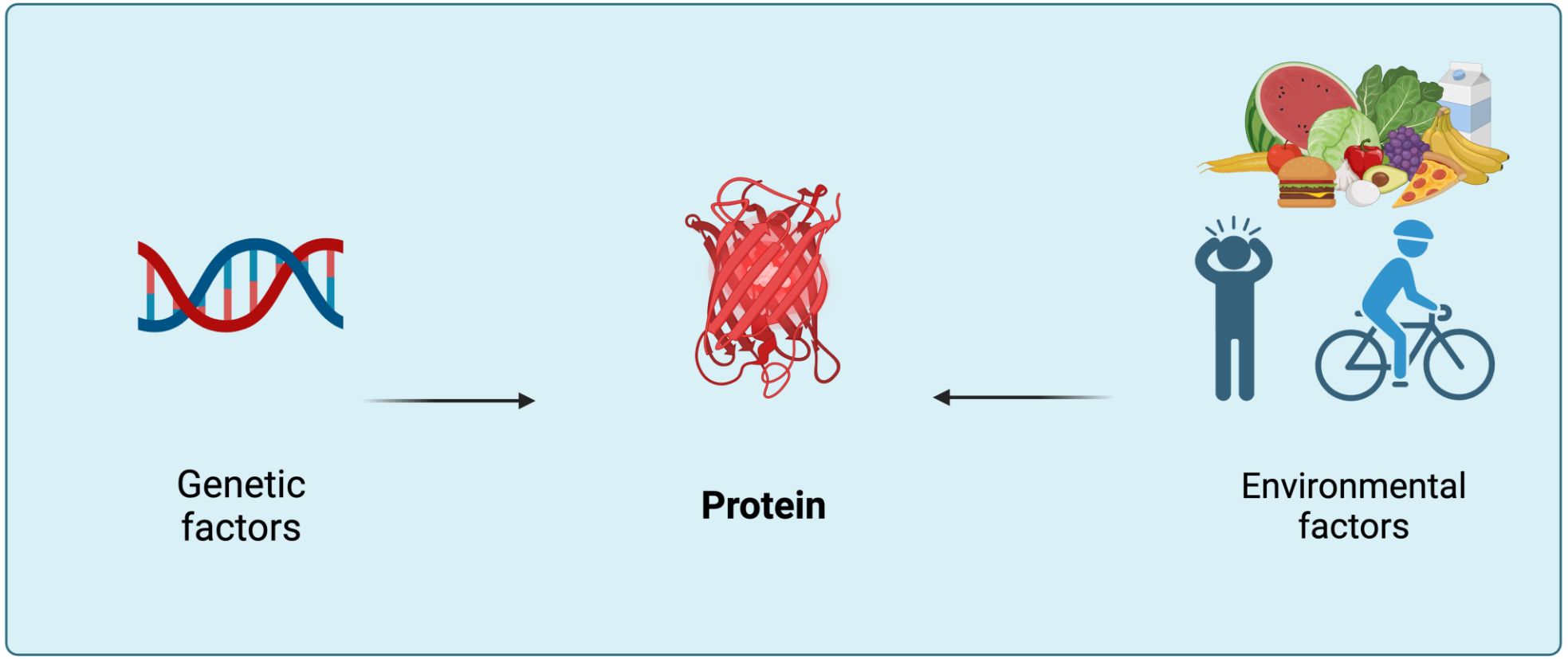
The test is intended to complement the company's TBI plasma test, which received FDA clearance in 2021.

Abbott has received clearance from the FDA for the first commercially available laboratory blood test for traumatic brain injury (TBI), according to a company press release.[1] The test, which will complement the company's rapid i-STAT TBI Plasma test, which received FDA clearance in 2021,[2] will run on Abbott's Alinity i laboratory instrument.

According to the press release, the test will give health care providers an objective way to quickly assess individuals with mild TBIs or concussion. The test measures 2 blood biomarkers that are "tightly correlated to brain injury." Test results are available within 18 minutes.

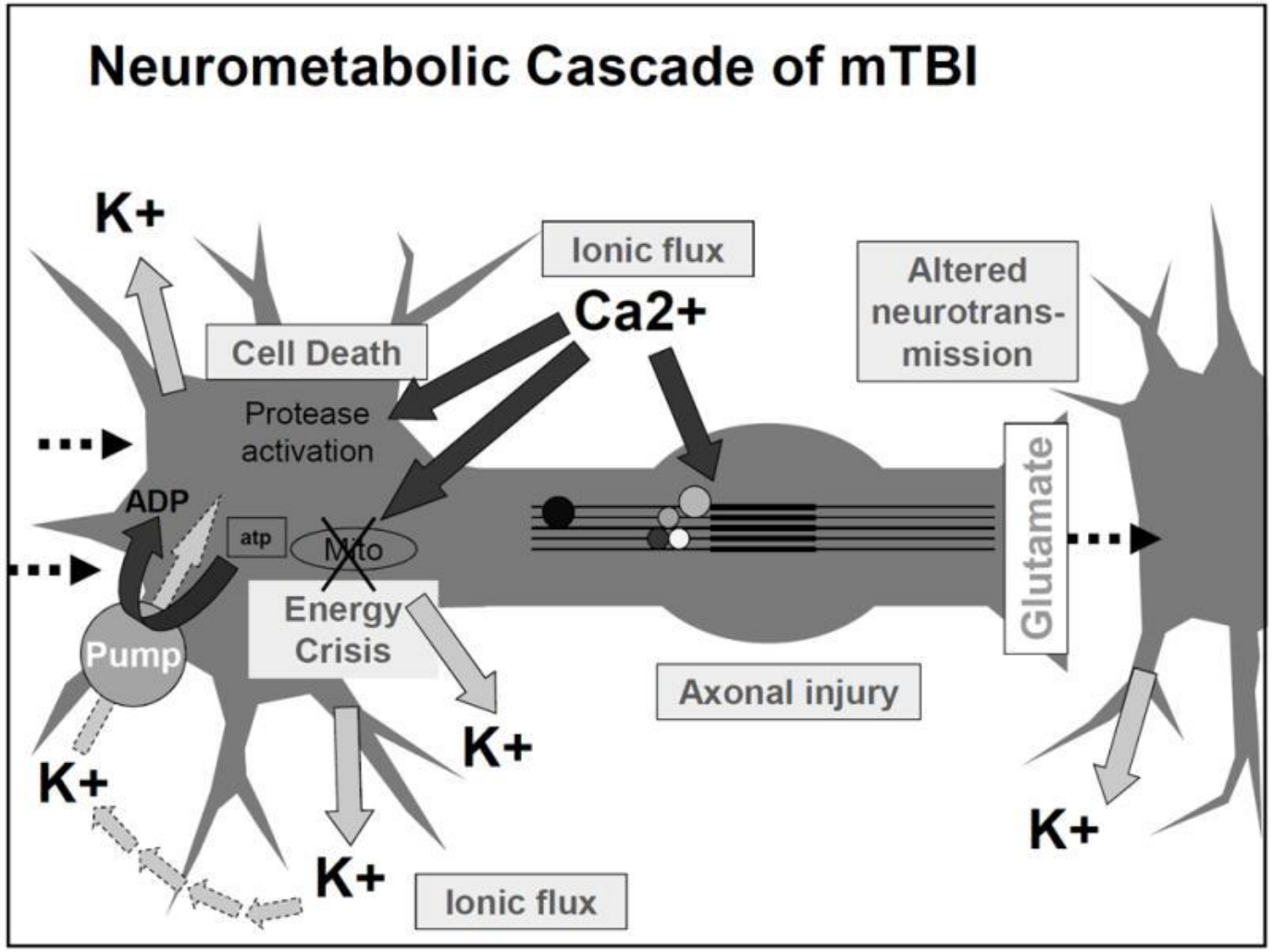
- Have you been involved in a blood biomarkers study before?
- Have you been involved in proteomics study before?
- Have you used a mass spectrometer before?

Proteomics is the study of the many hundreds and thousands of proteins in a sample



[1]Wu et al. 2011 Journal of Dental Research
[2]Van Eyk & Snyder 2019 Journal of Proteome Research

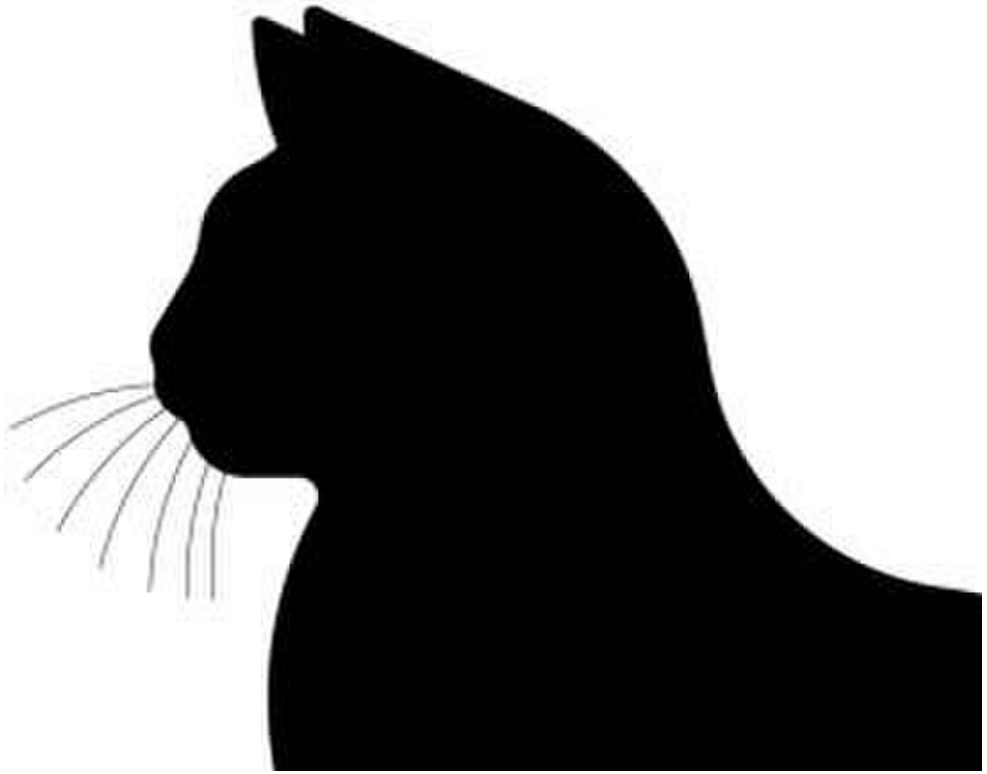
Why proteomics in concussion?

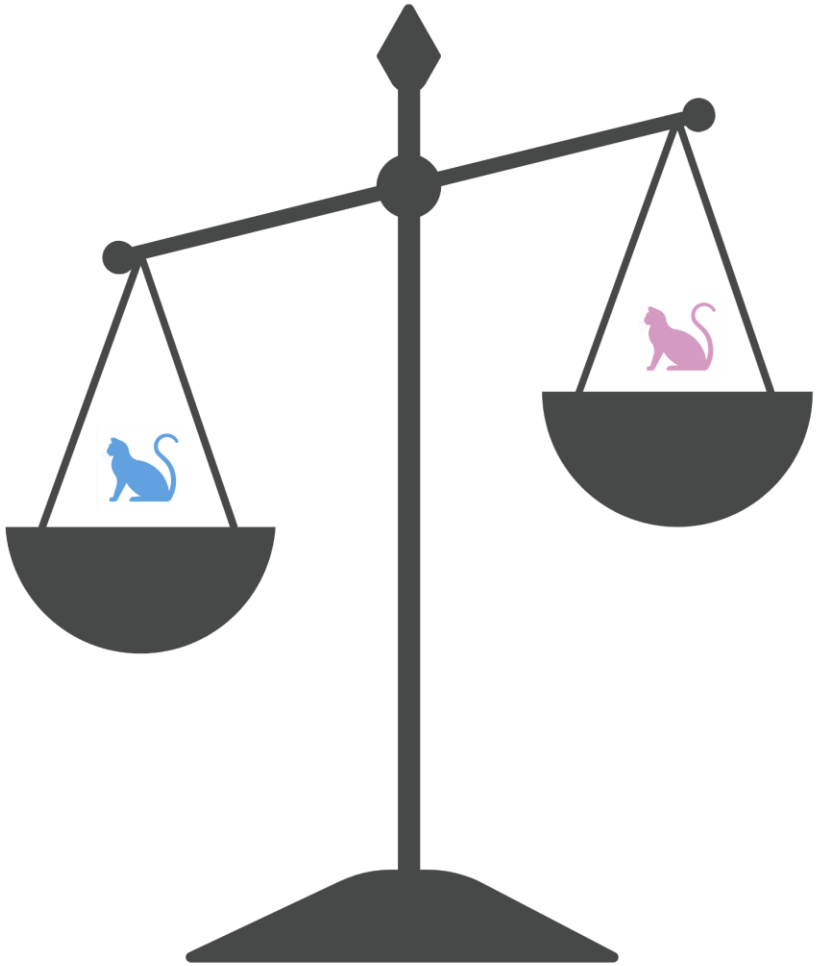


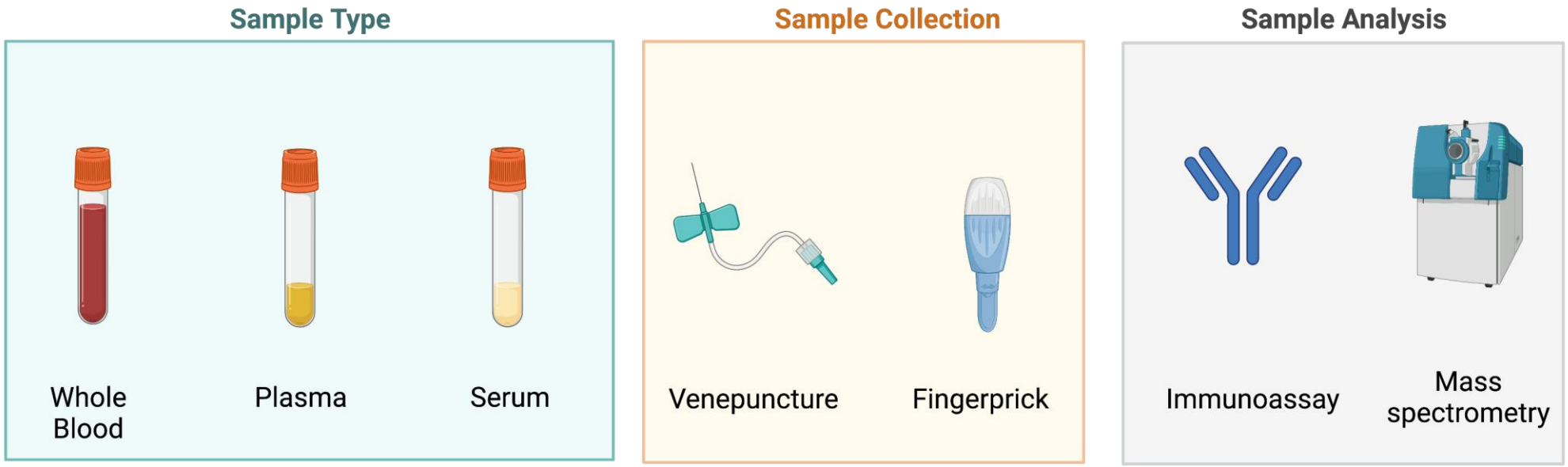
What about recovery?

1. Giza et al., 2014

Proteomic blood markers of delayed recovery from concussion in children







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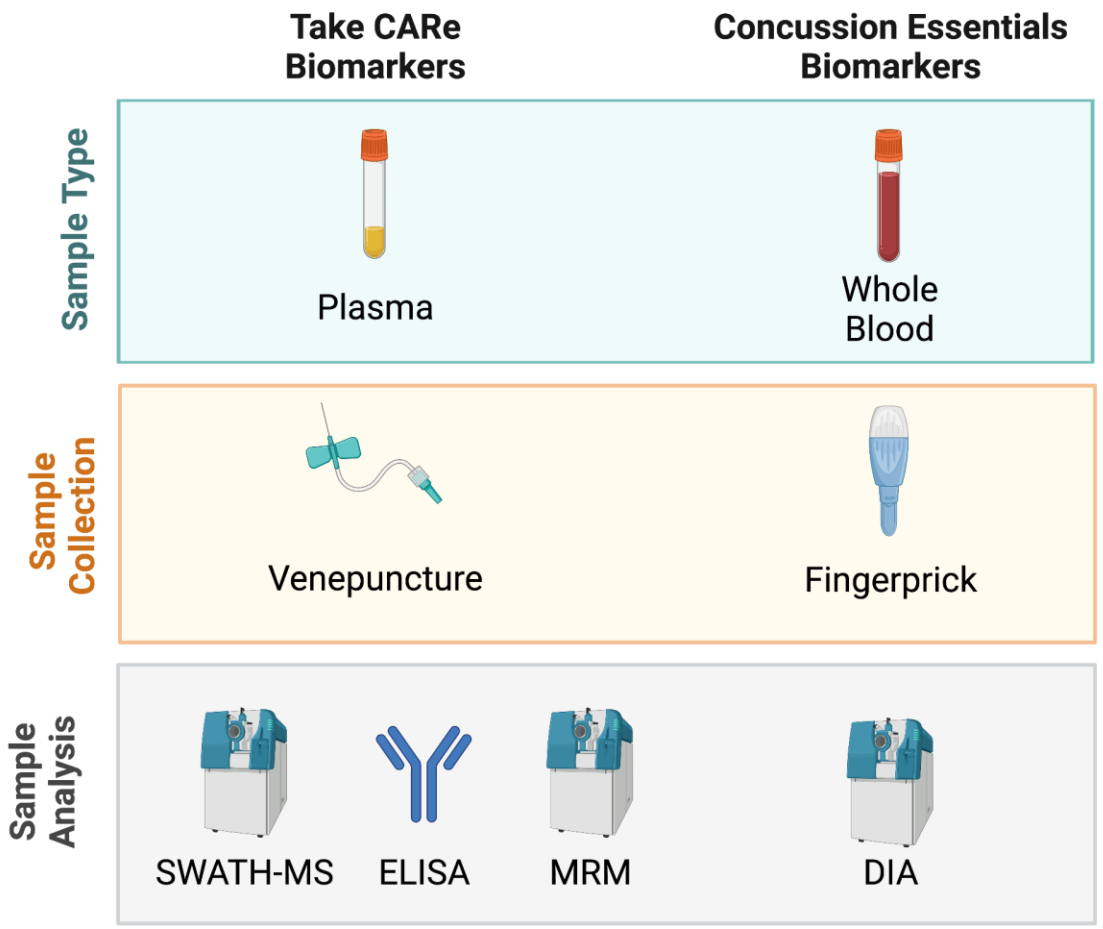
Our Studies

1. Take CARe Biomarkers: Plasma markers of delayed recovery from concussion in children[1]

2. Concussion Essentials Biomarkers: Capillary markers of delayed recovery from concussion in children

1. Takagi et al., 2019



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2

Take CARe Biomarkers:

Discovery of alpha-1-antichymotrypin as a marker of delayed recovery from concussion in children

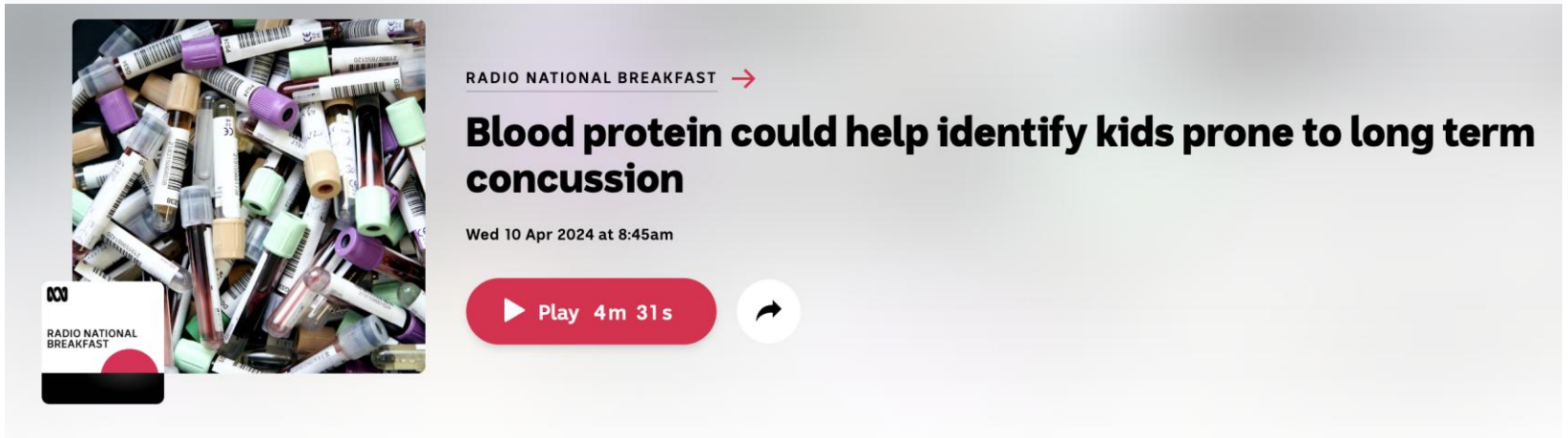
Journal of Neurotrauma > Vol. 41, No. 19-20

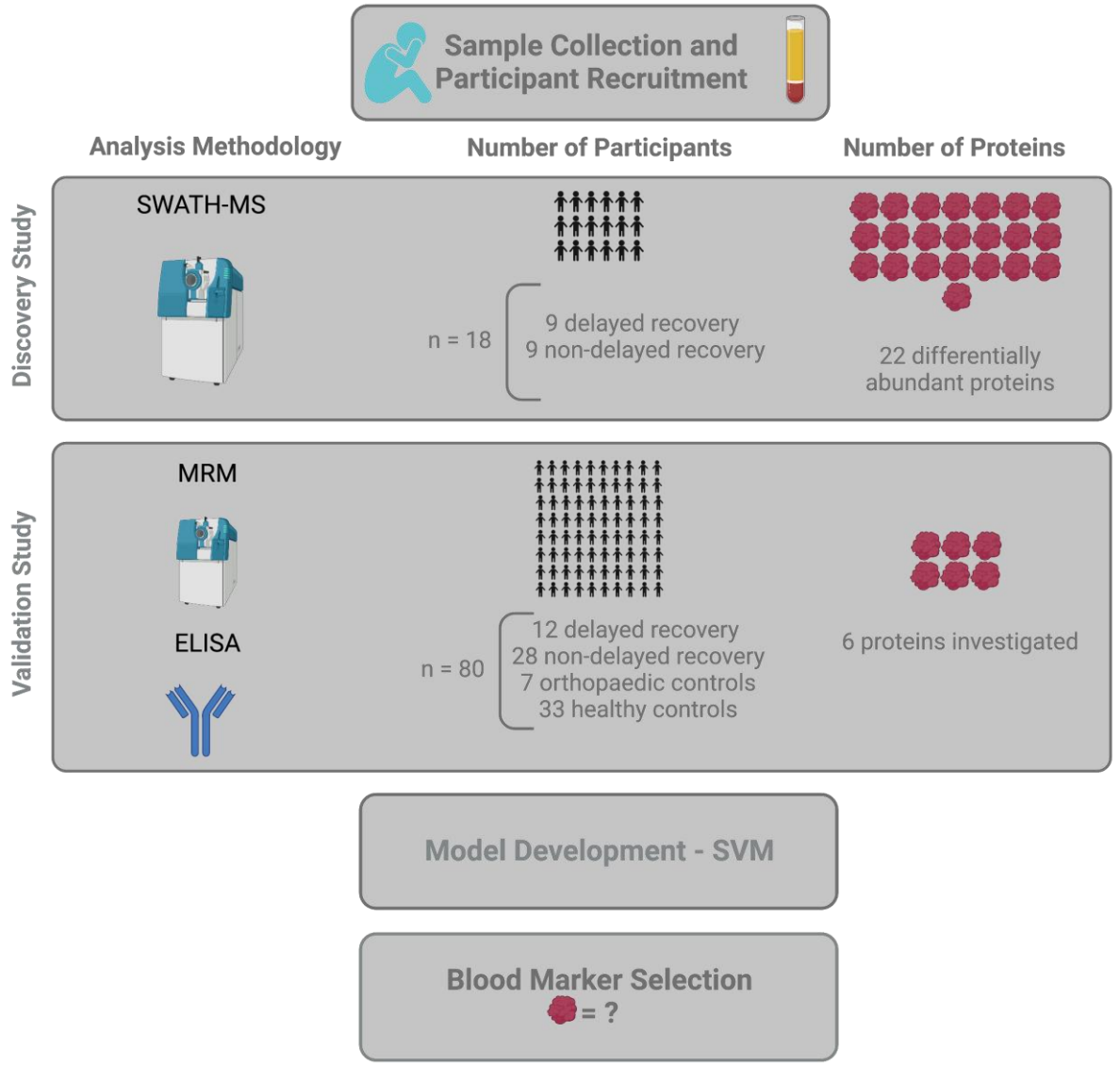
Research Article | FULL ACCESS | Published Online: 21 October 2024

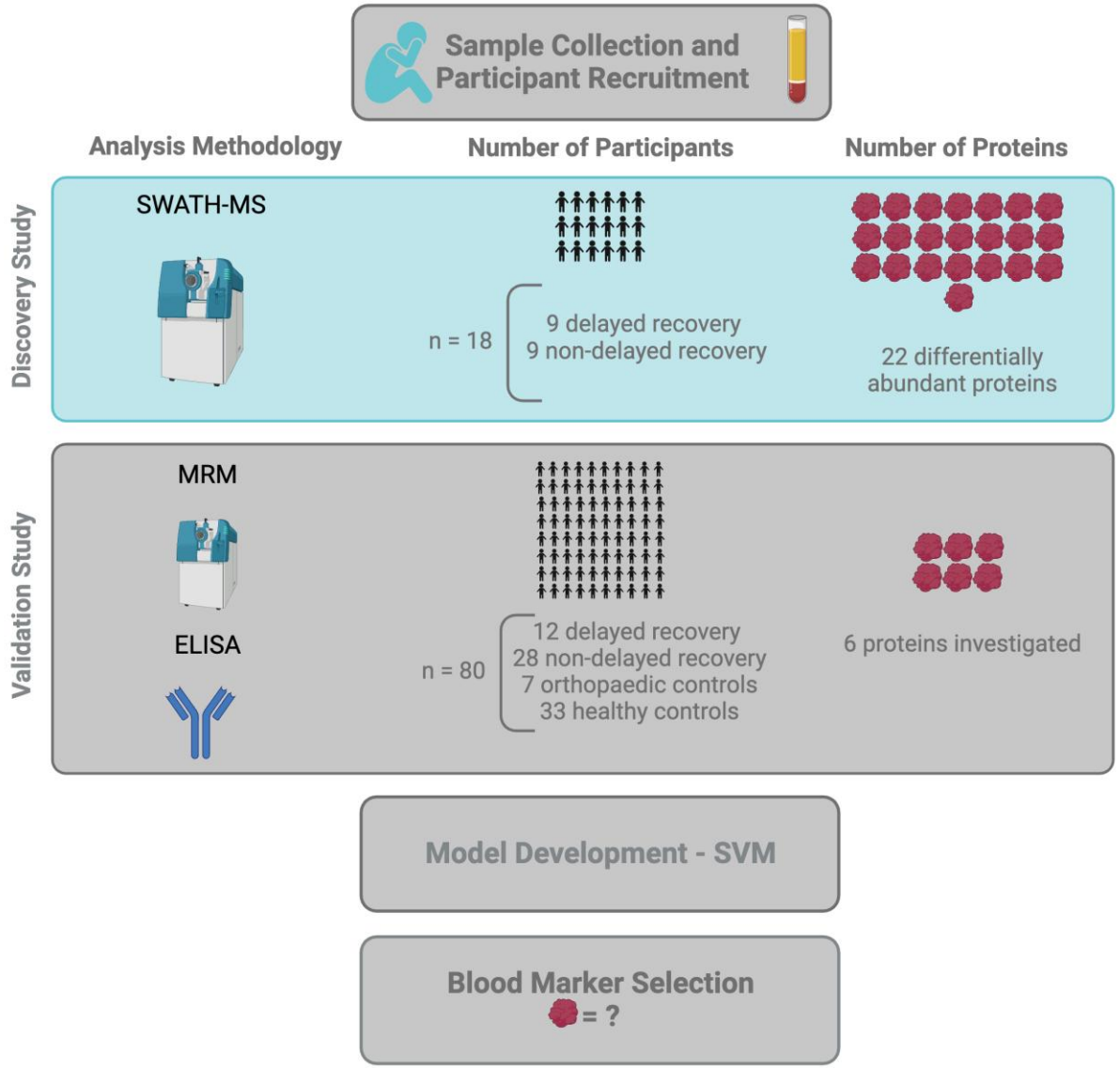
Discovery of Alpha-1-Antichymotrypsin as a Marker of Delayed Recovery from Concussion in Children

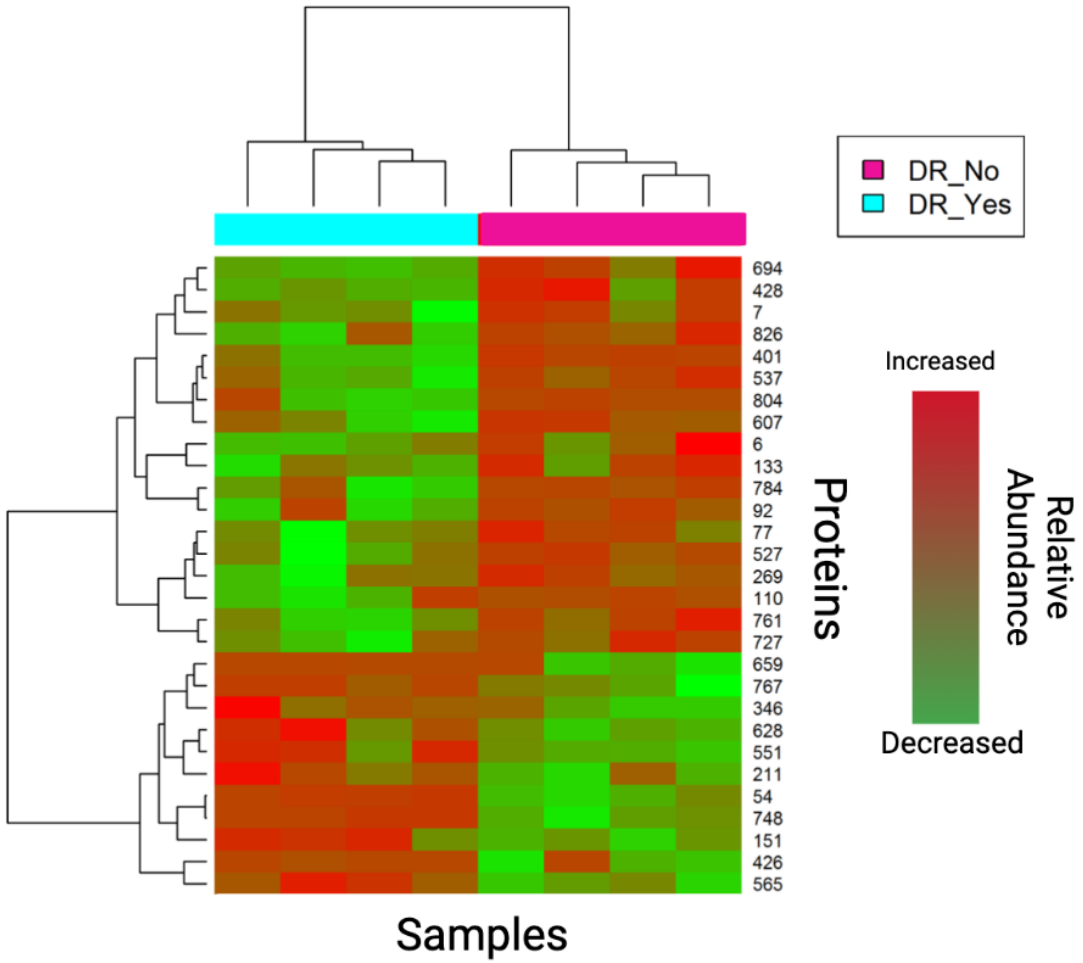
Authors: Ella E.K. Swaney, Franz E. Babl, Vanessa C. Rausa, Nicholas Anderson, Stephen J.C. Hearps, Georgia Parkin, Gene Hart-Smith, ... SHOW ALL ..., and Vera Ignjatovic | AUTHORS INFO & AFFILIATIONS

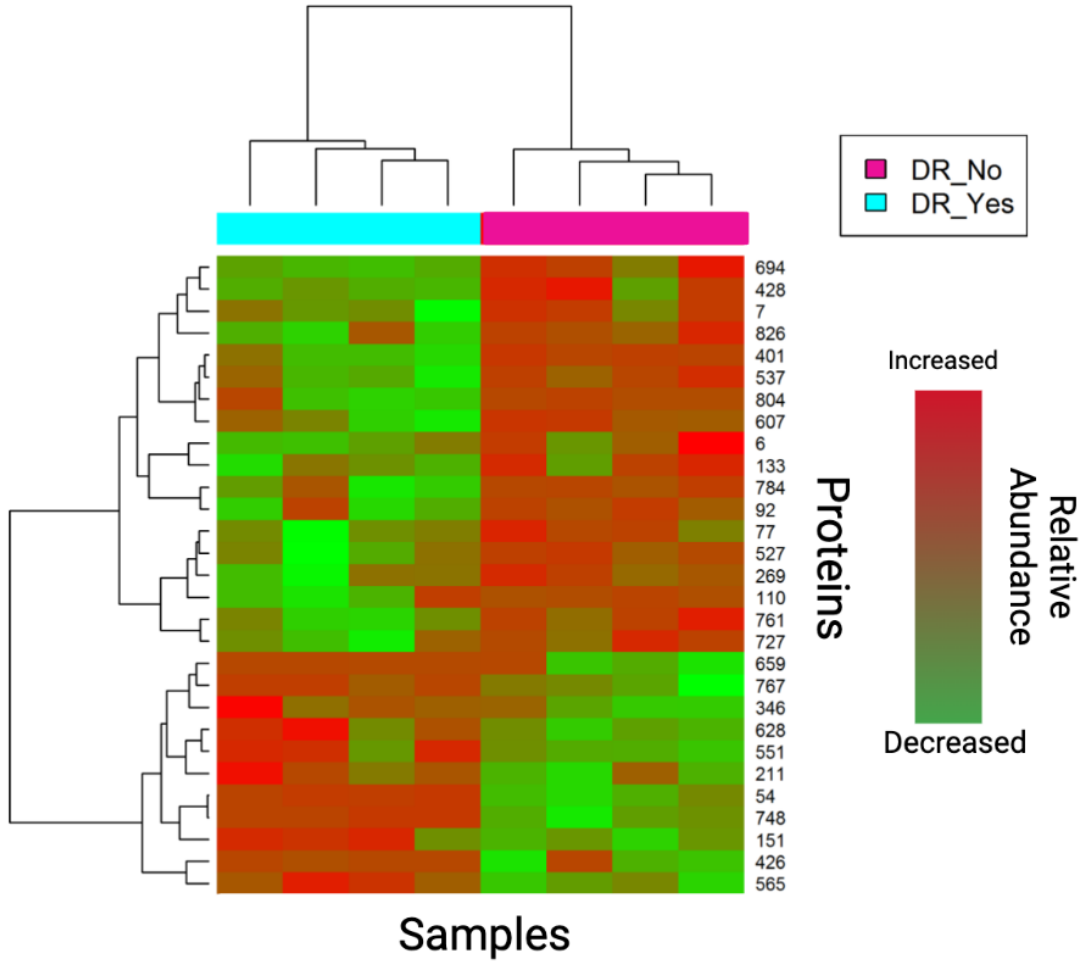
Publication: Journal of Neurotrauma • https://doi.org/10.1089/neu.2023.0503



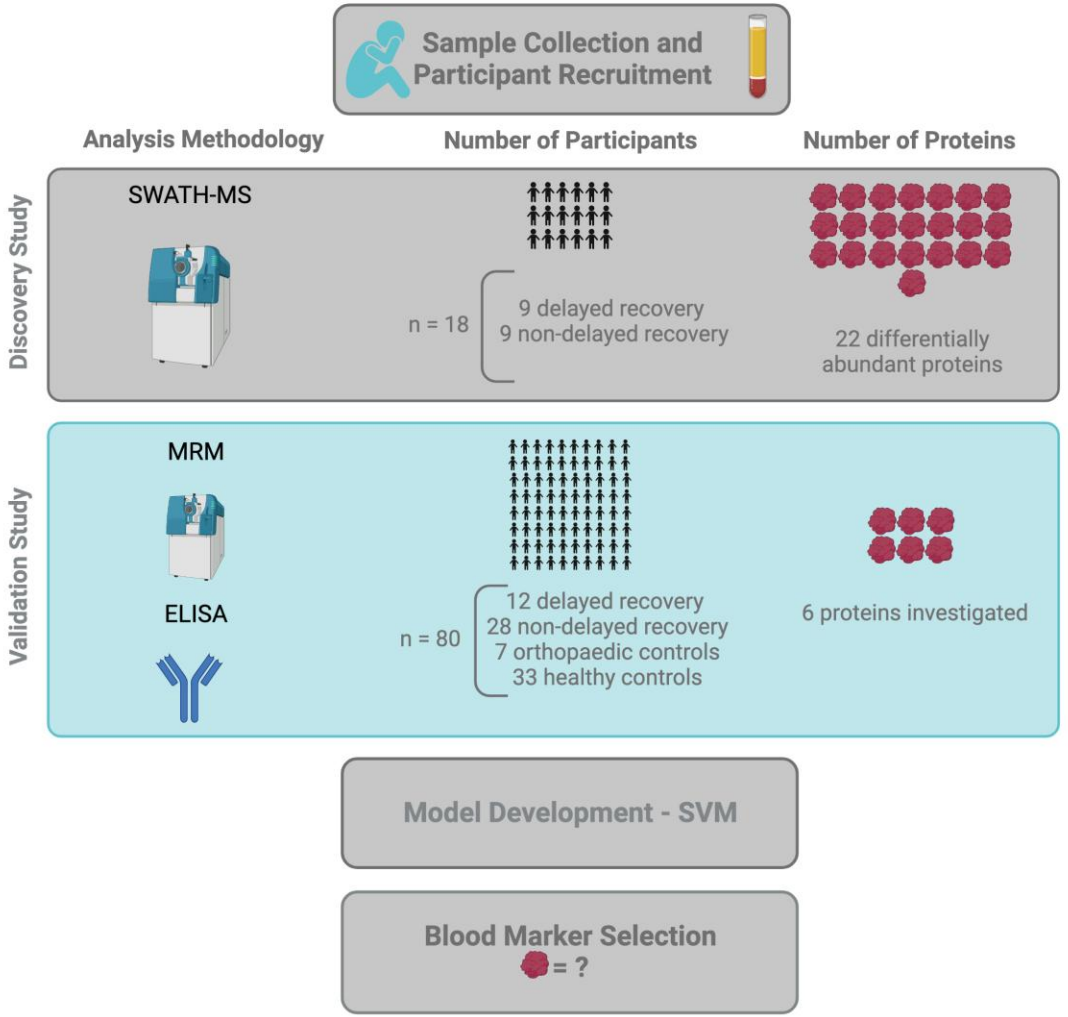


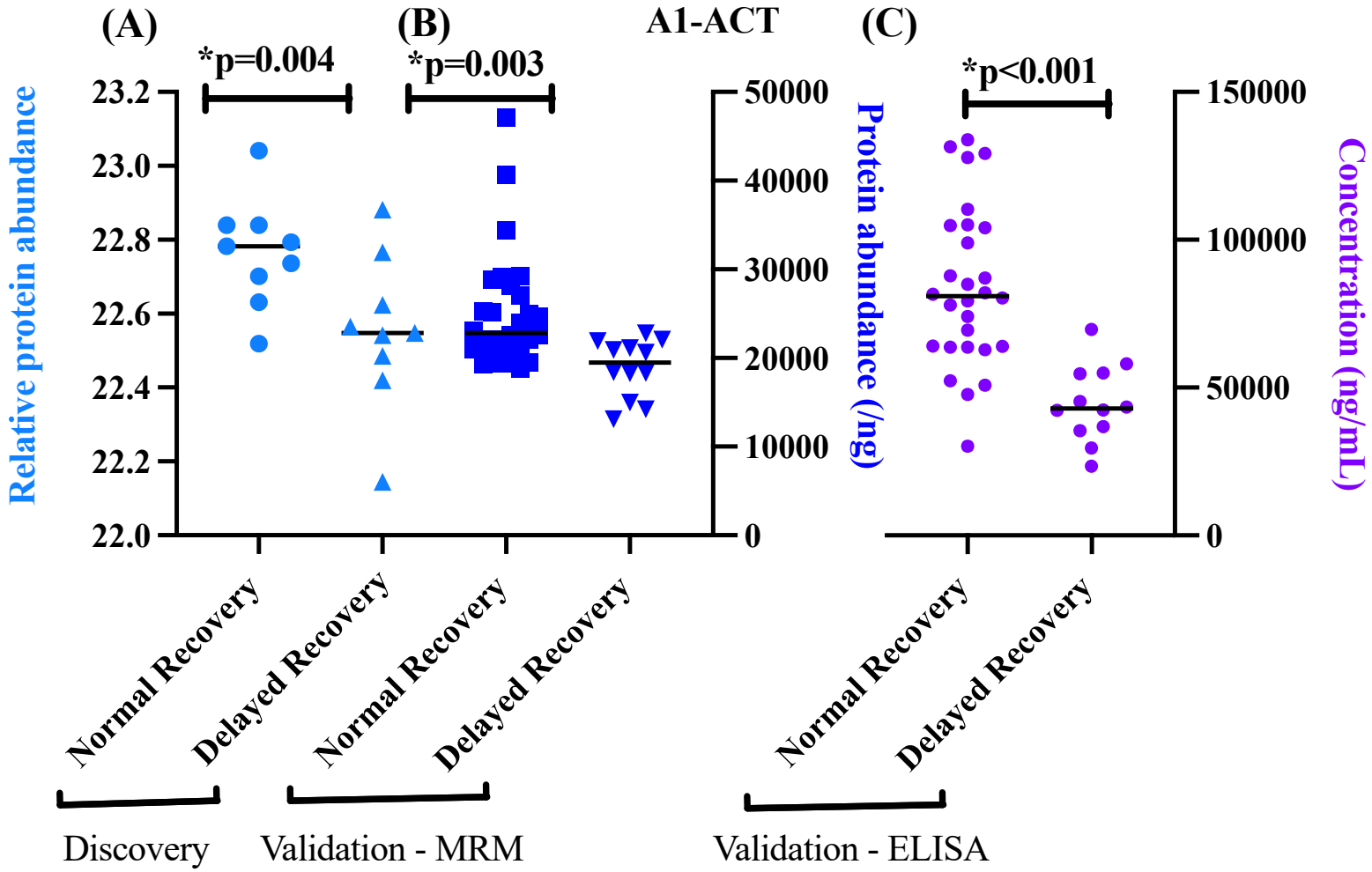






22 Proteins → 6 Proteins

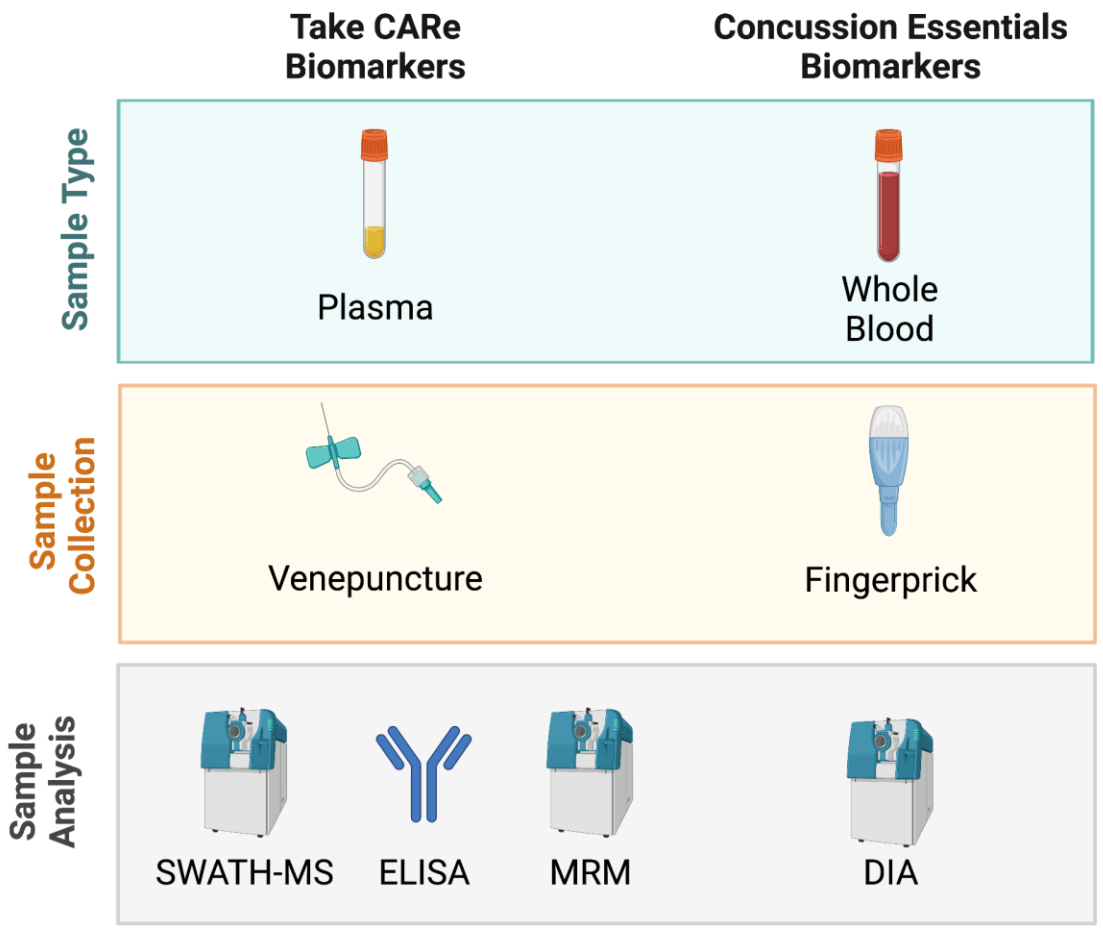




- Alpha-1-ACT is a candidate marker of delayed recovery from concussion in children
- Inflammatory acute phase serum glycoprotein[2]
- Higher in participants with severe & moderate BI compared to mTBI[1]

1. Anada et al. 2018

2. Padmanabhan et al. 2006



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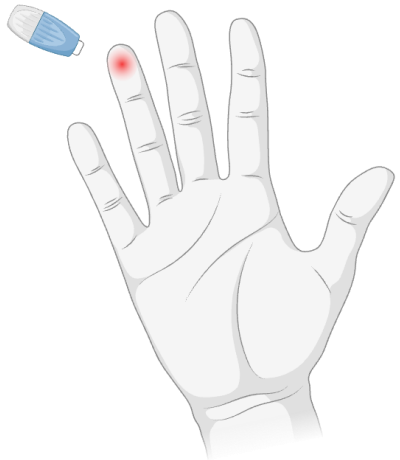
3

Concussion Essentials Biomarkers:

Capillary Blood Markers of Delayed Recovery from Concussion in Children

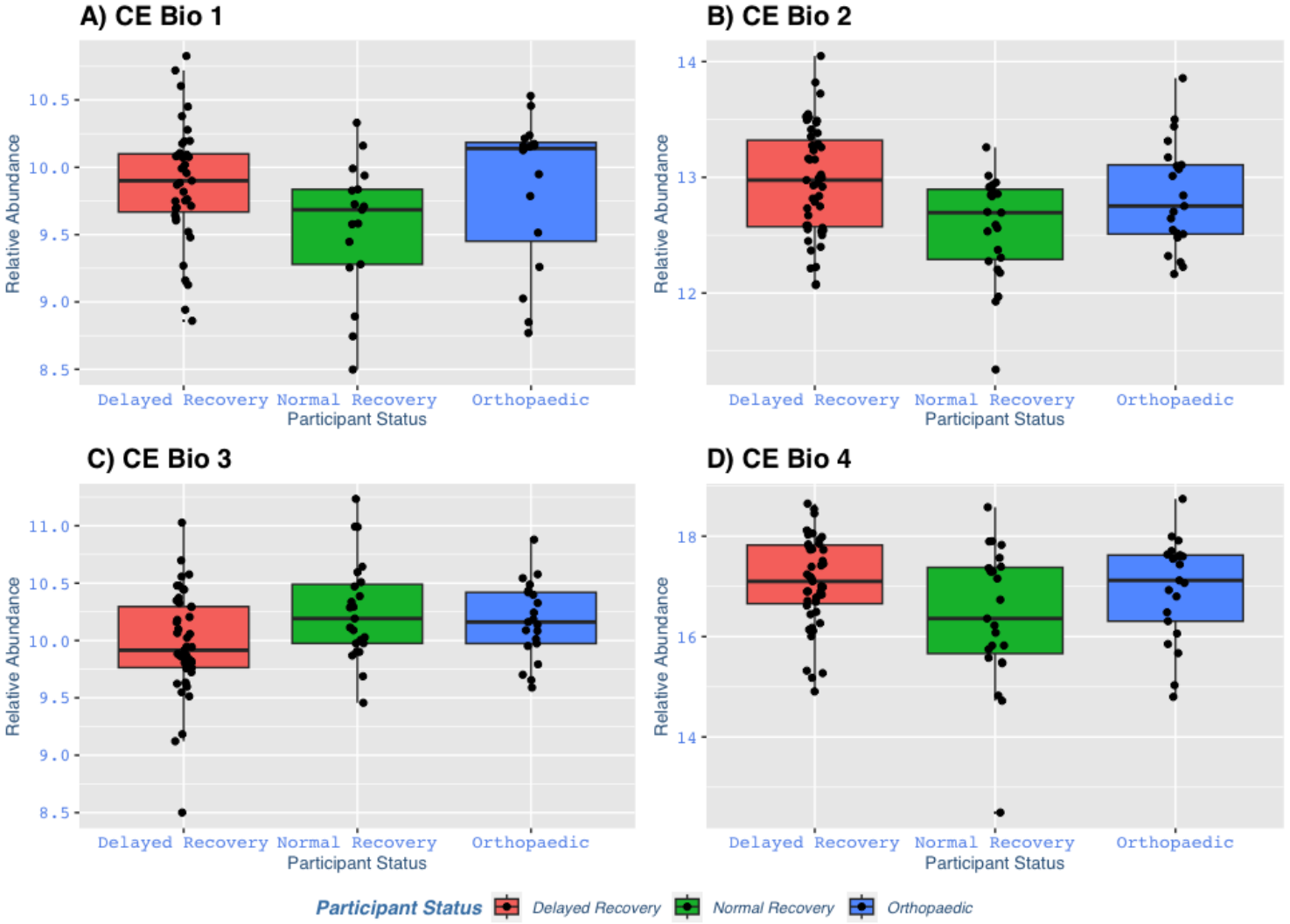
The Mitra Microsampling Device (Mitra Clamshell)



Participant Demographics

	Orthopaedic Controls	Normal Recovery	Delayed Recovery	Concussion - Missing outcome	Total
N	21	23	47	12	**103**
Females: n (%)	8 (38.1)	6 (26.09)	11 (23.40)	6 (50.00)	**31 (30.10)**
Age: mean, years, range, years	13.24 8.0 – 16.0	11.96 8.0 – 15.0	13.00 9 – 17.0	13.50 8.0 – 17.0	**12.87** **8.0 - 17.0**

92% consent rate



Key Takeaways - Sample Collection

Venepuncture

- Large sample volumes
- Less impacted by contaminants

- Uncomfortable
- Inconvenient

Fingerprick

- Convenient – used in community
- Painless - better in paediatric settings
- Doesn’t require clinician involvement
- Cost effective

- Less developed technology
- Small sampling = more easily contaminated
- Cannot collect plasma or serum

Clinical Implications

- Candidate markers in **venous** and **capillary** blood of delayed recovery from concussion in children

- Utilises novel methological approaches – sample collection and analysis

Future Directions

- Continuation of Concussion Essentials Biomarkers study
- Healthy reference ranges for candidate markers in venous and capillary blood
- Sidelines, point of care, rural & remote collection

murdoch children's research institute

Thankyou