New approaches for monitoring changes in disease in myeloproliferative neoplasms

MPN Education Symposium

25th October 2025

Dr Belinda Guo

Translational Cancer Pathology Laboratory

School of Biomedical Sciences, University of Western Australia

tcpl-sbms@uwa.edu.au

Acknowledgement of Country

We acknowledge the traditional custodians of country throughout Australia and their continuing connection to land, sea, and community. We pay our respect to Elders past, present, and emerging, including those of the Whadjuk people of the Noongar nation, the traditional owners of the lands where we are meeting today.

Disease progression in MPN

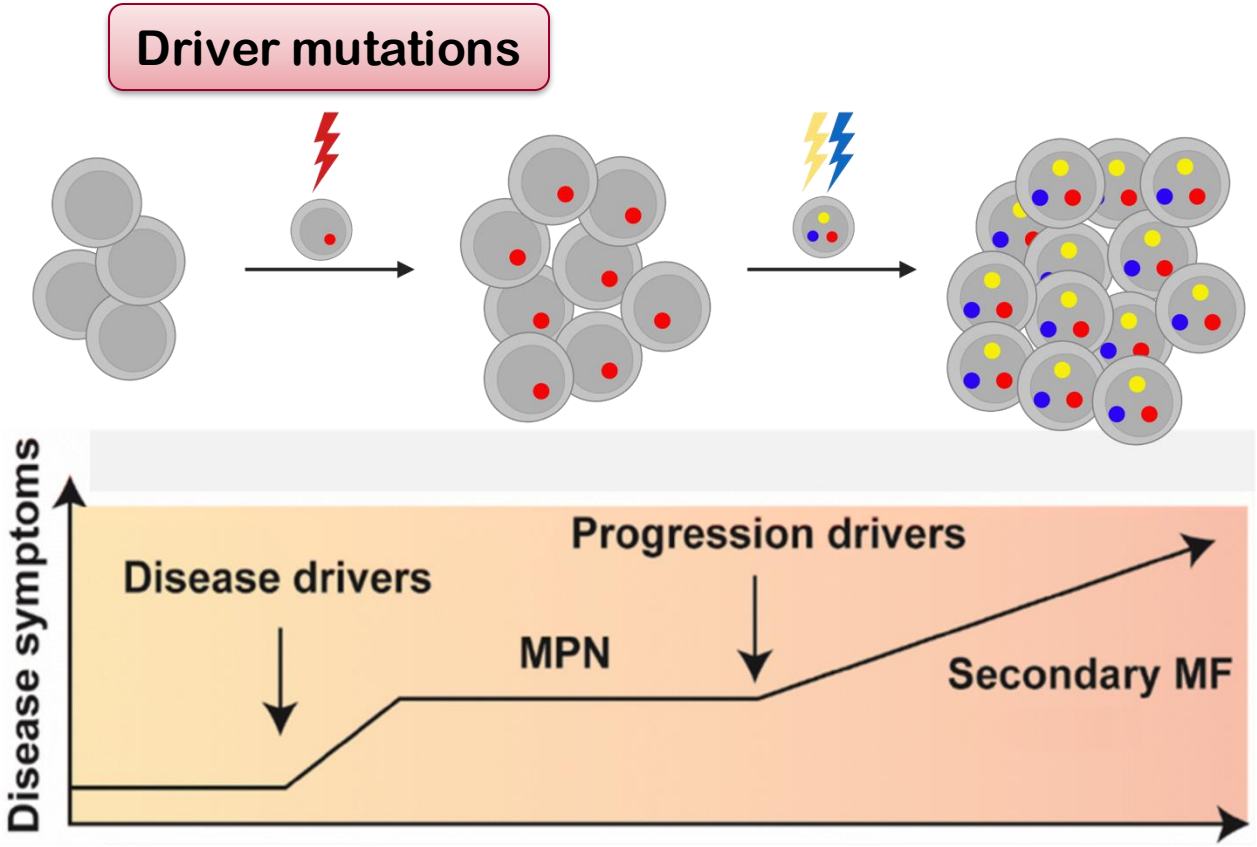
- Essential thrombocythemia (ET) and Polycythemia vera (PV) carries a small risk of progression to myelofibrosis (MF)

A need for new ways to identify progression earlier so doctors can hopefully intervene

Created in BioRender.com

What causes progression to MF?

- We do not know the exact mechanism yet, but we have gained insights from studies and identified genetic changes in DNA that are associated with progression



Mutations in other genes that changes:

- the way the DNA is read
- what part of the DNA is read
- the order for how the DNA is read

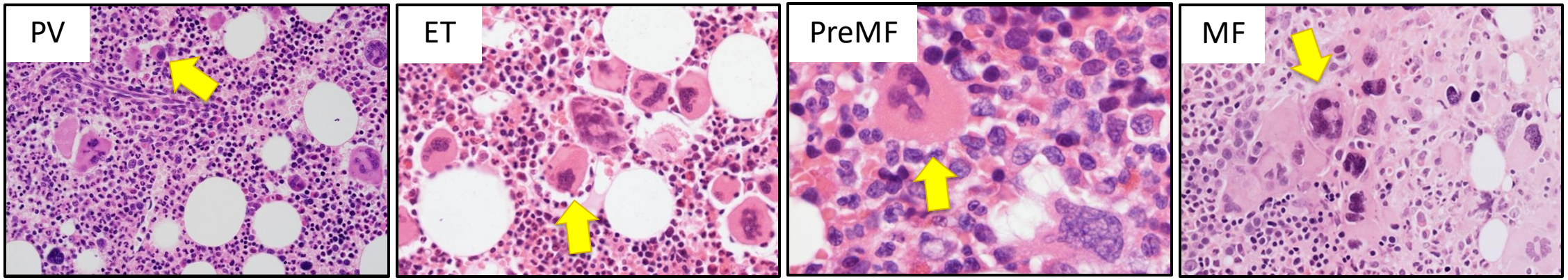
→ Abnormal expression of genes that change the way the cell behaves

These mutations increase risk, but do not predict progression

Jia & Kralovics, Int J Hemat 2020; Tefferi et al, Blood Cancer J 2023

A new approach to find markers of MF

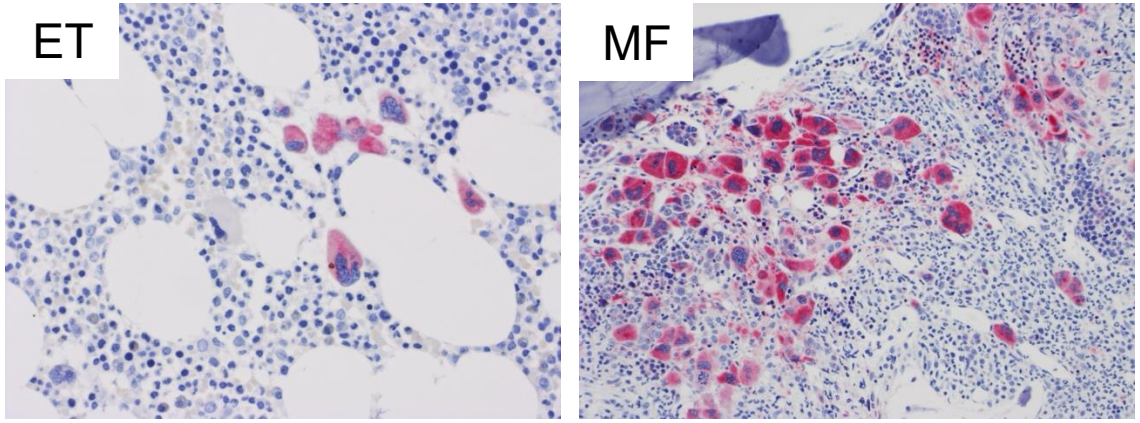
- Megakaryocytes are large cells in the bone marrow that make platelets (for clotting) and maintain general bone marrow health
- There are distinct changes in megakaryocytes with progression to MF (e.g. the number, shape, size and location in the marrow)
- Studies have shown these cells can induce deposition of reticulin fibres (scarring of the marrow), which is characteristic of MF

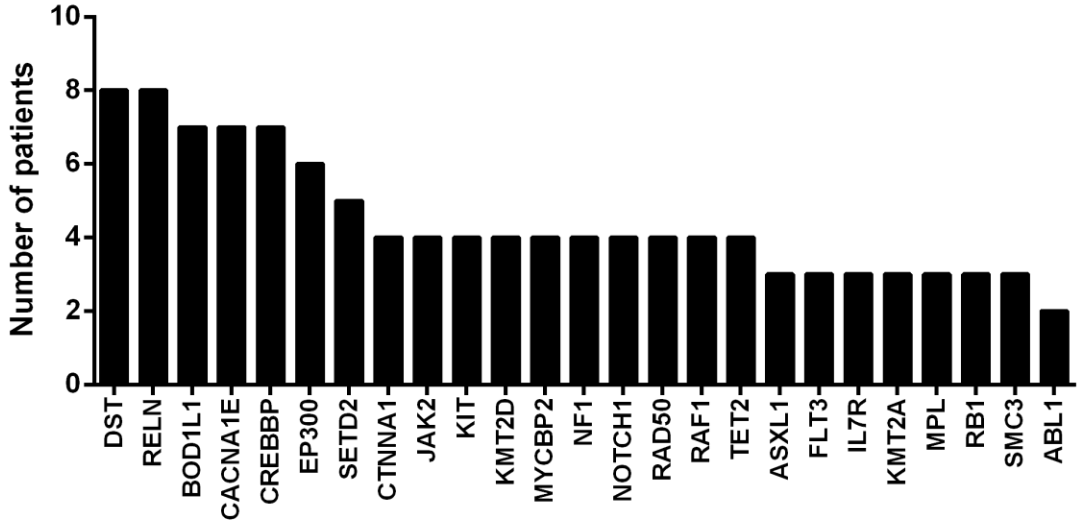


Ng et al, Int J Lab Hematol 2023

Megakaryocytes in MPN

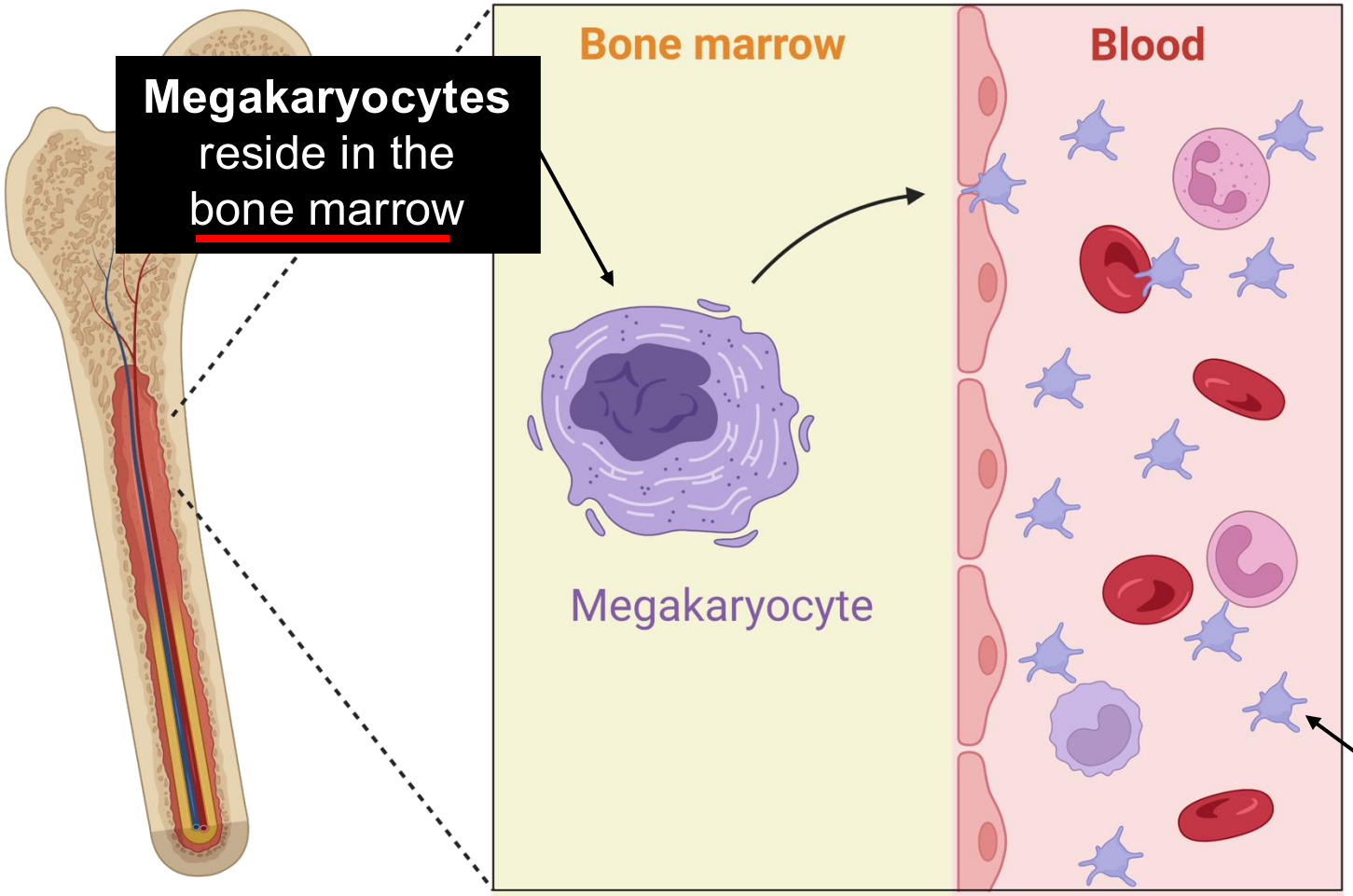
- We studied megakaryocytes from patient bone marrow samples
- Megakaryocytes in MF had uncontrolled growth
- Megakaryocytes in MPN have unique mutations, which is higher in number and burden in MF
- This suggested that these cells have an “unstable” genome that might be responsible for the abnormal features seen in MPN and MF





Malherbe et al, J Clin Pathol 2016; Guo et al, Am J Pathol 2017

From the bone marrow to the blood



Megakaryocytes reside in the bone marrow

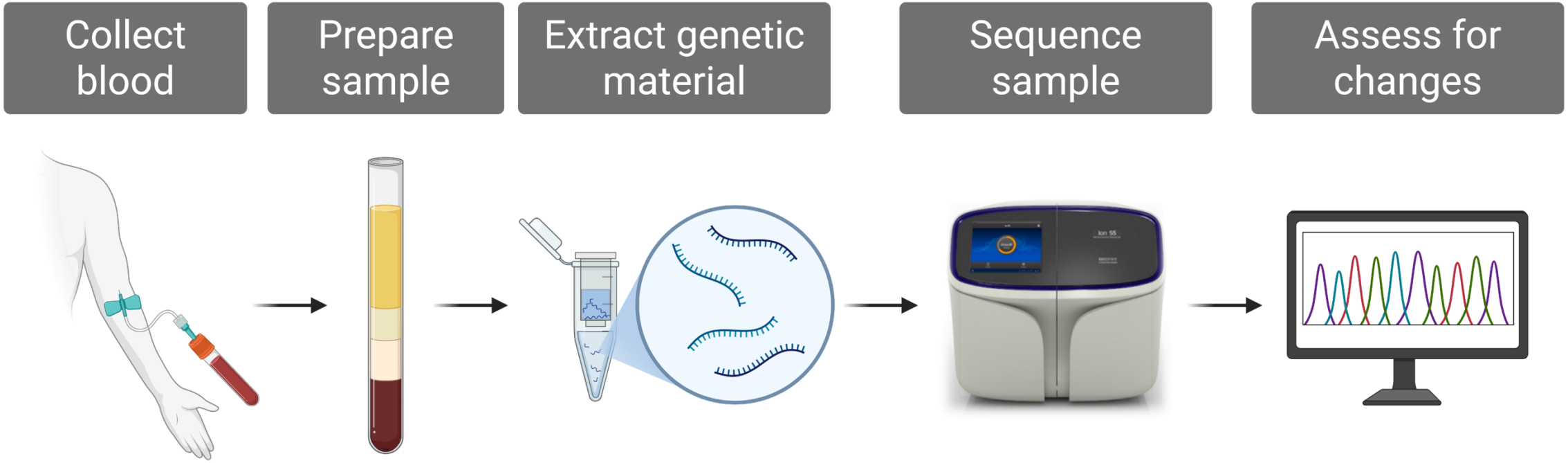
Can we detect genetic changes that are associated with MF by looking at platelets in the blood?

Platelets are made by megakaryocytes and released into the blood

Created in BioRender.com

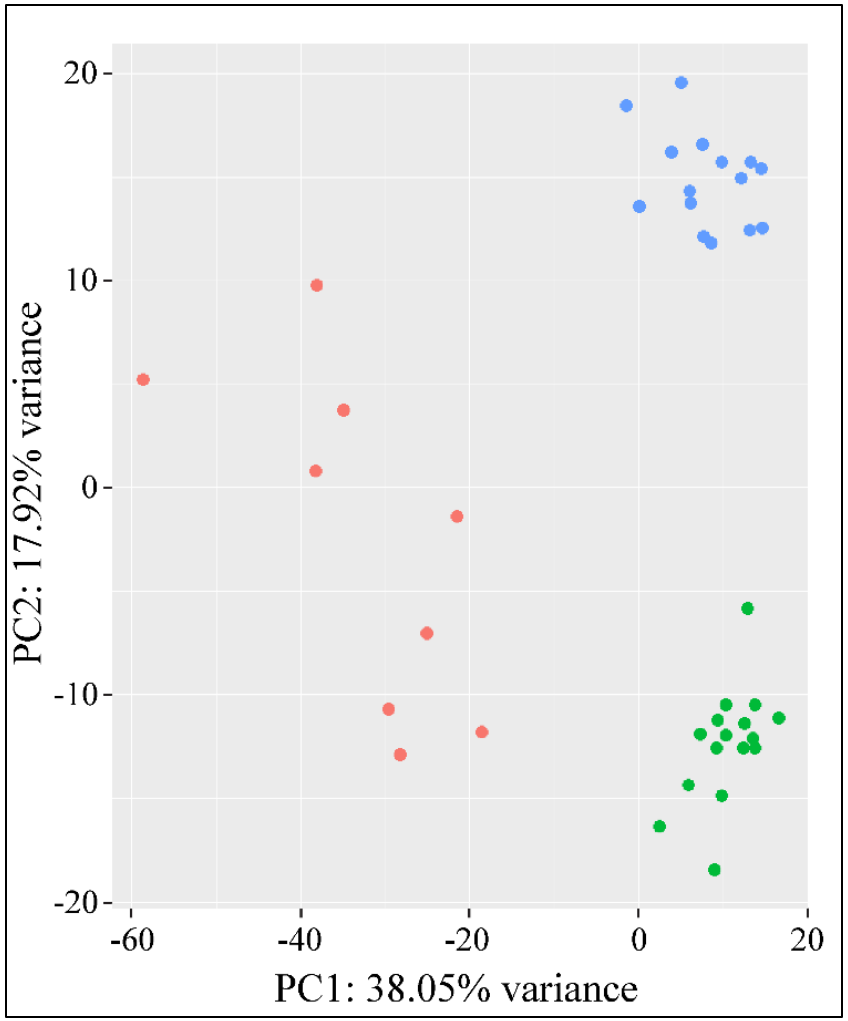
How we analyse platelets

- Our translational research project is active and recruiting participants and collecting samples from consenting patients at Royal Perth, Fiona Stanley, Rockingham and Sir Charles Gairdner Hospitals



Project Title: Determining novel markers of bone marrow failure in myeloproliferative neoplasms (RGS-3807)

Distinct genetic changes in platelets in MF

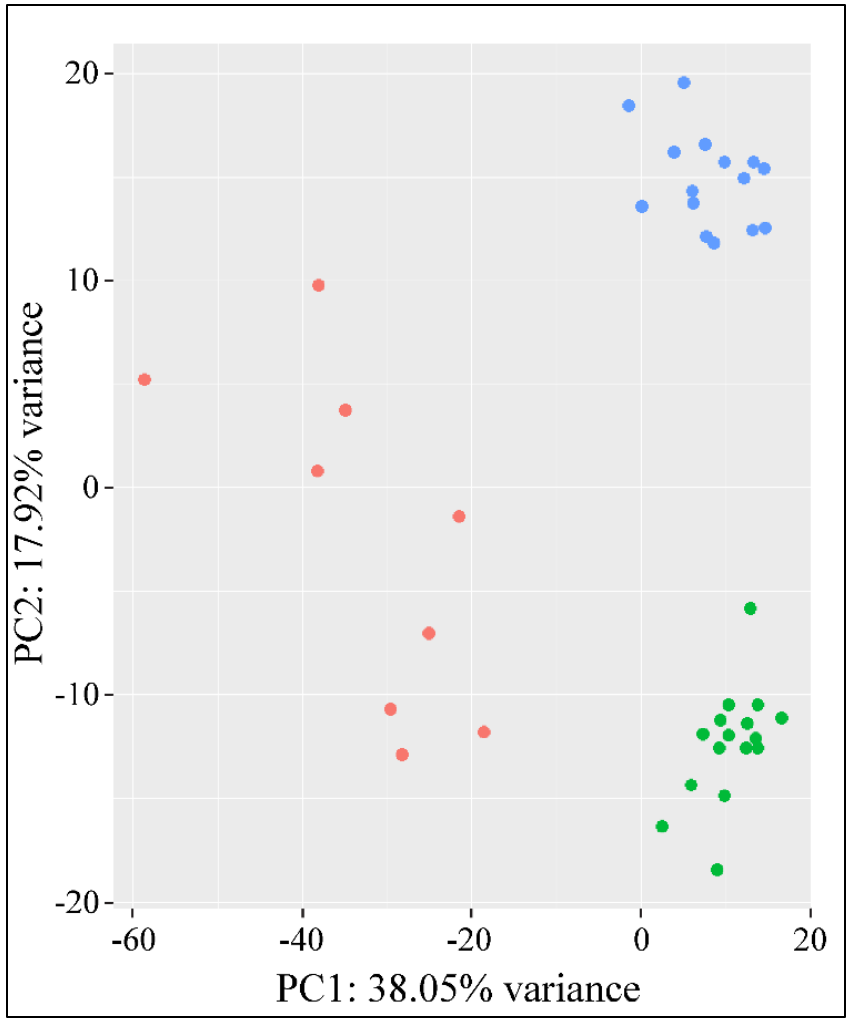


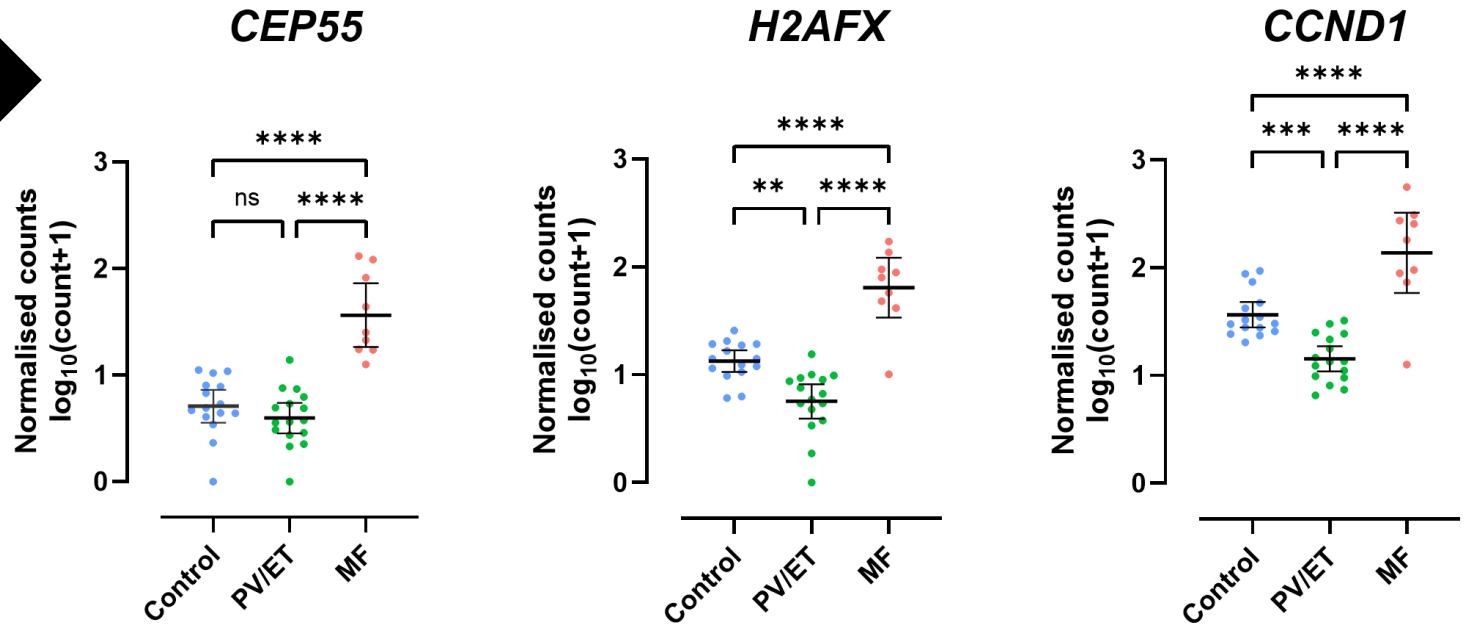
- Samples from individuals without MPN (control)
- Samples from individuals with ET or PV
- Samples from individuals with MF

- There are distinct changes in platelets from patients with MPN compared to controls
- Further, there are additional changes in platelets from patients with MF compared to those with ET and PV
- This suggests that platelets contain disease-specific changes that may be helpful for monitoring changes in disease status in MPN using just blood

Guo et al, BJH 2020

Distinct genetic changes in platelets in MF





- There are a lot of genetic changes in platelets in MF
- Increased expression of these genes is specific to MF
- Looking for changes in these genes over time may help with disease monitoring and potentially detect progression earlier

Guo et al, BJH 2020; Collinson et al, Methods 2023

Platelet signature for MF – next steps

- Platelets in MPN have distinct genetic changes and have potential as a convenient tool for monitoring disease status

PV/ET	*PREDICTING*	*DETECTING* MF	*MONITORING*	Disease response
	• Early intervention & access to trials • Increase quality of life (reassurance)		• Less invasive (blood testing) • Drug efficacy (are normal processes being restored?)	

Provide timely information to clinicians → improve outcomes for patients

Acknowledgements

Patients and their families!

University of Western Australia
Ryan Collinson
Lynne Wilson
Ruby Hamilton
Kathy Fuller
Wendy Erber
Matthew Linden
Past and present members of TCPL

Department of Health WA
Hun Chuah
Zi Ng
Michael Leahy
Rebecca Howman
Carolyn Grove
SCGH Haematology
RPH Haematology
RGH Haematology

Community Representatives
Nathalie Cook
Sue Taylor
Jenny Myers

tcpl-sbms@uwa.edu.au

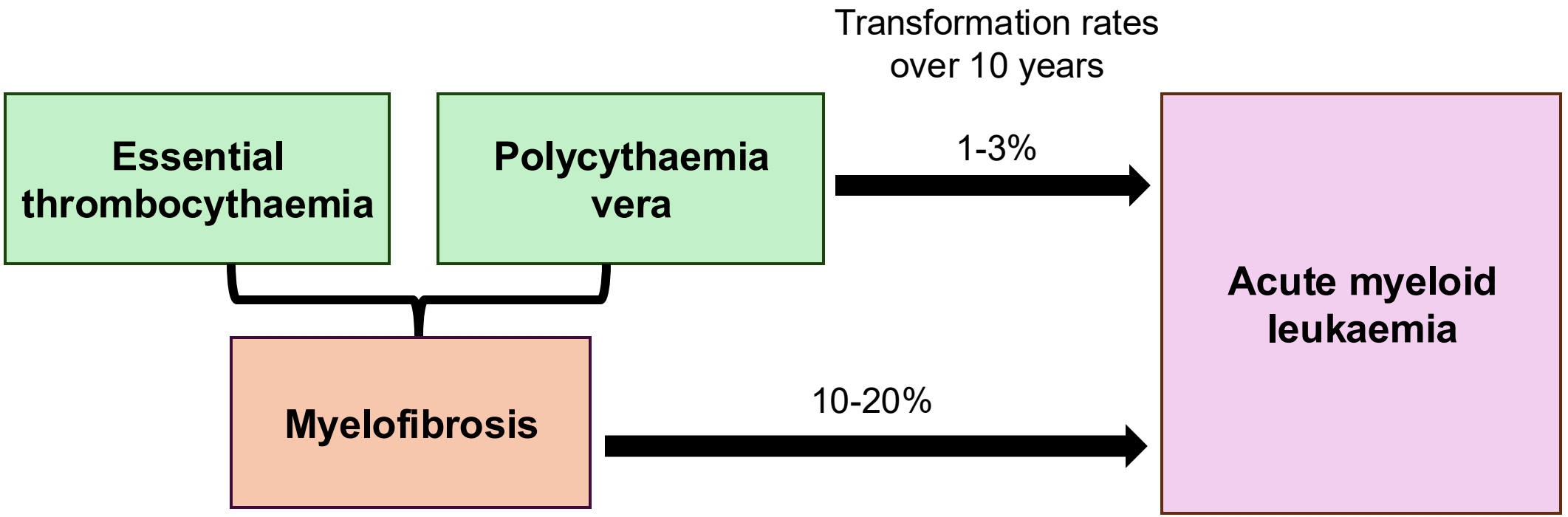
Predicting and Preventing MPN Disease Progression

Ruby Hamilton

2nd Year PhD Student

School of Biomedical Sciences, UWA

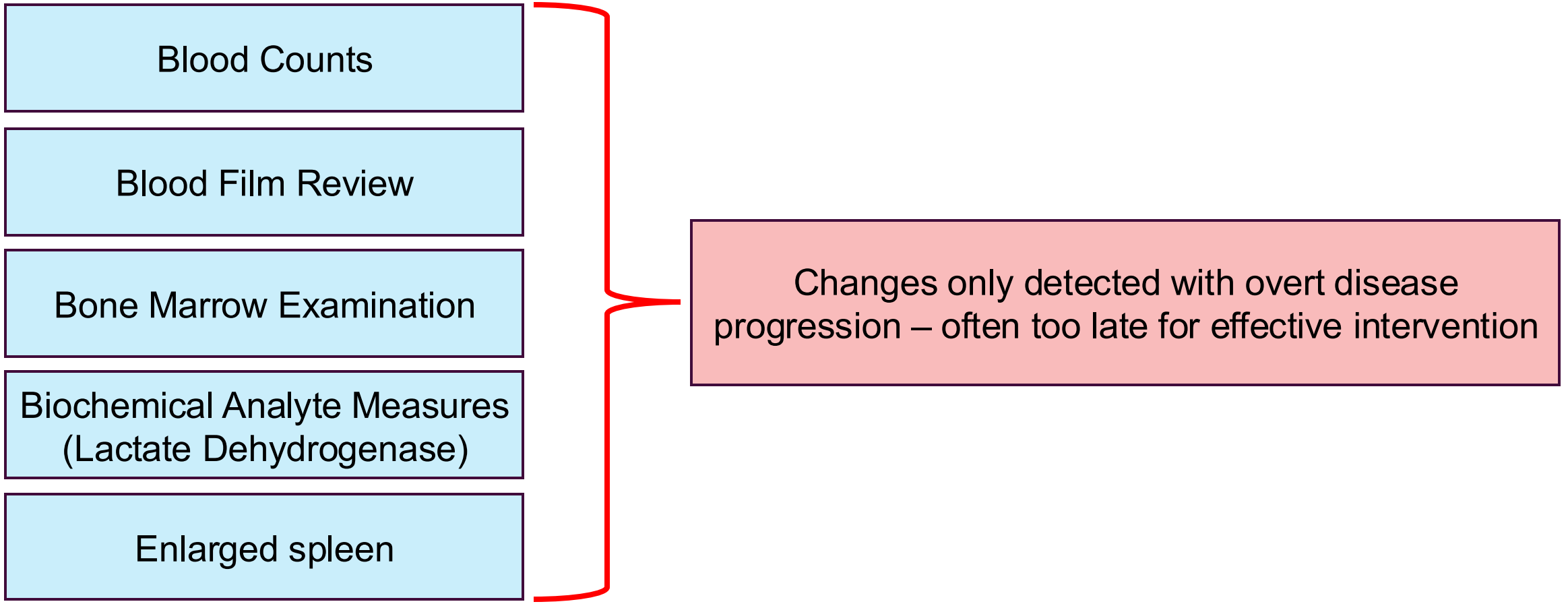
MPN Disease Progression



The biological pathways driving disease progression are not well understood

How can we identify patients at risk of MPN disease progression?

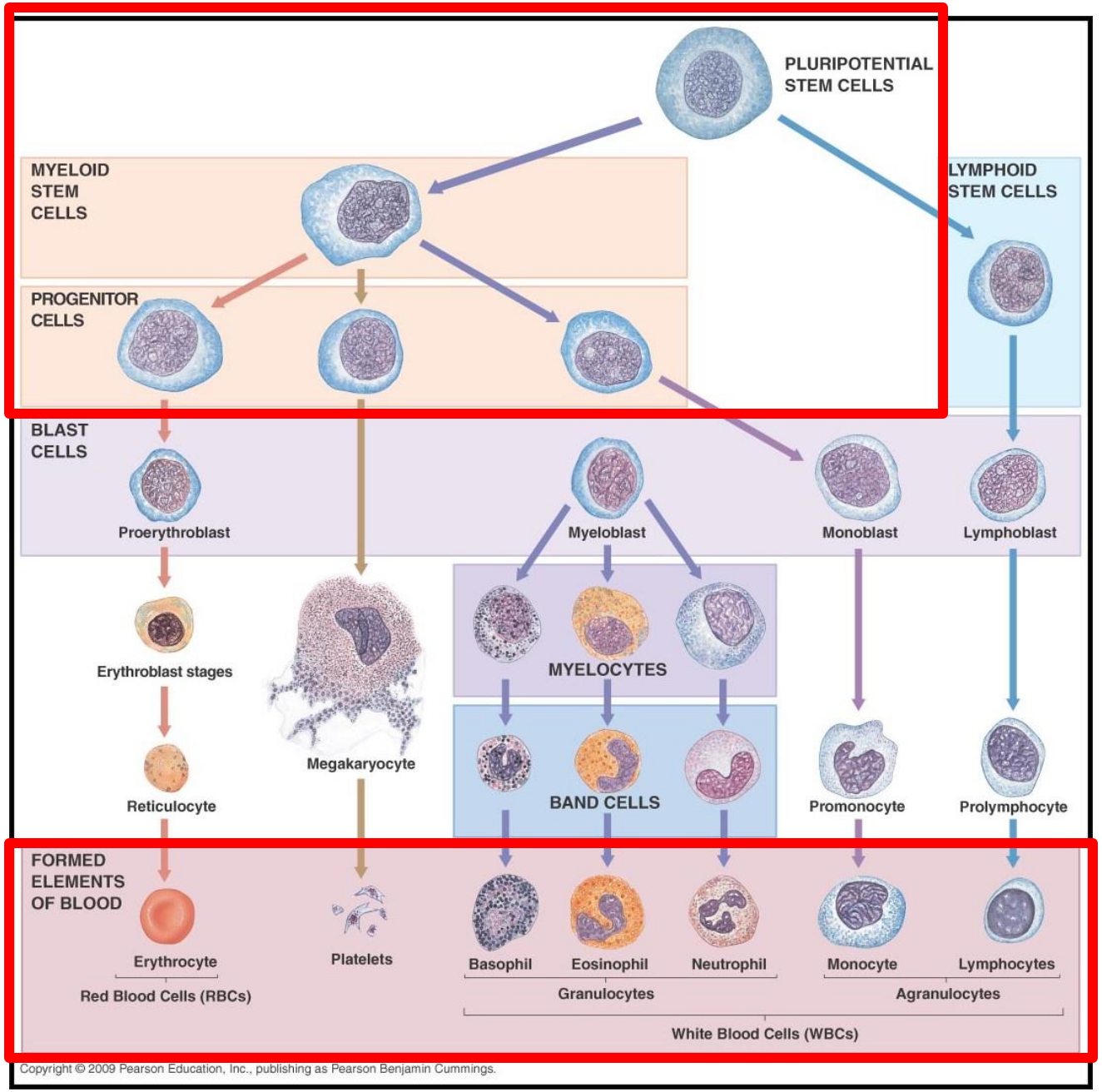
Detecting Disease Progression: Current Methods



How can we improve?

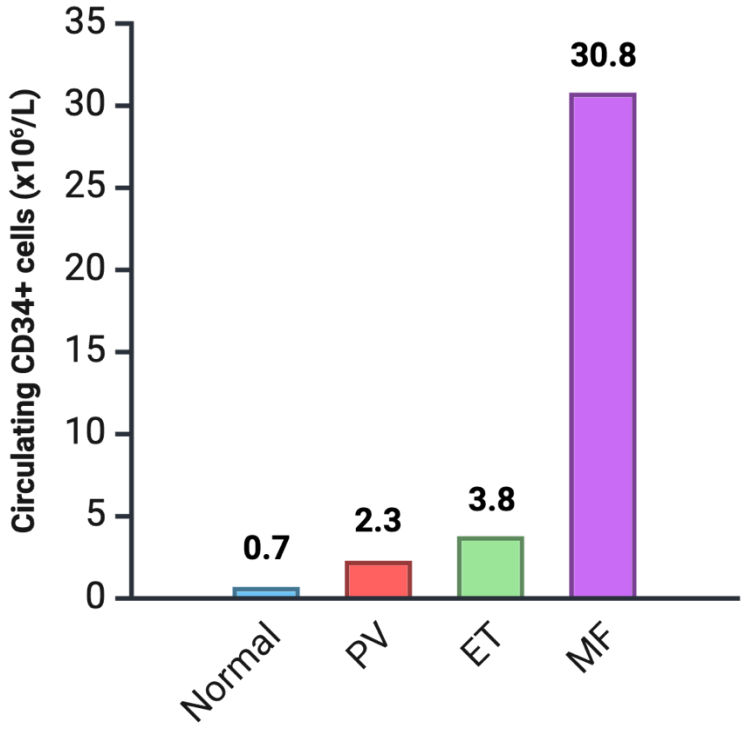
Immature Blood Cells

- Produce all blood cells
- MPN: RBCs, WBCs, platelets affected
- Genetic changes likely arose in the precursor cells



Immature Blood Cells

- Identified by expression of surface protein = "**CD34-positive**"
- Normally reside in the bone marrow → rare in the blood
- MPN → elevated levels in the blood
- Rising levels linked to disease progression

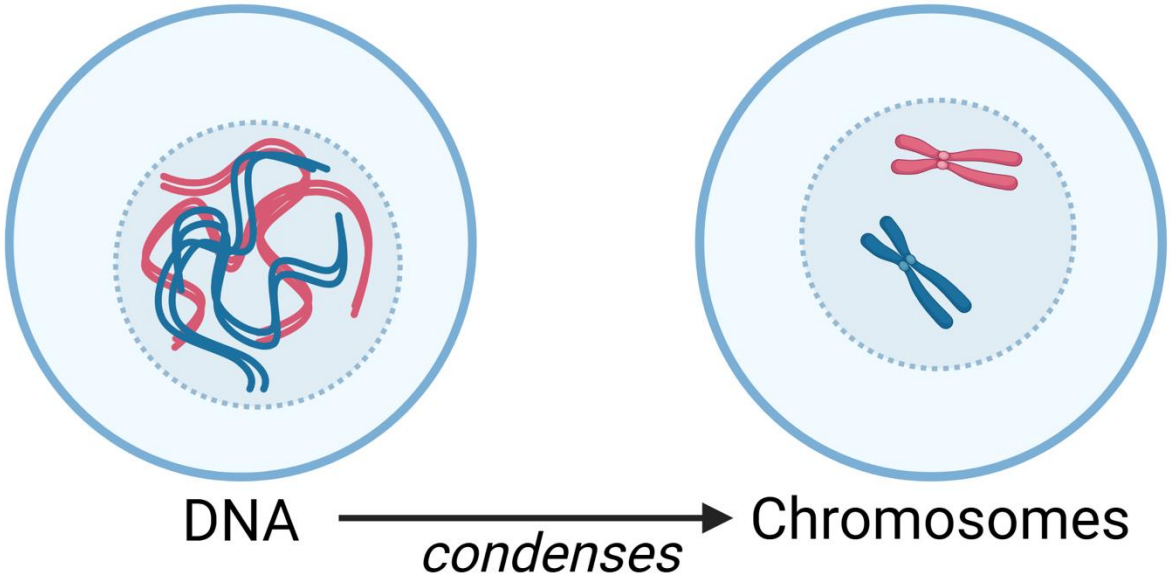


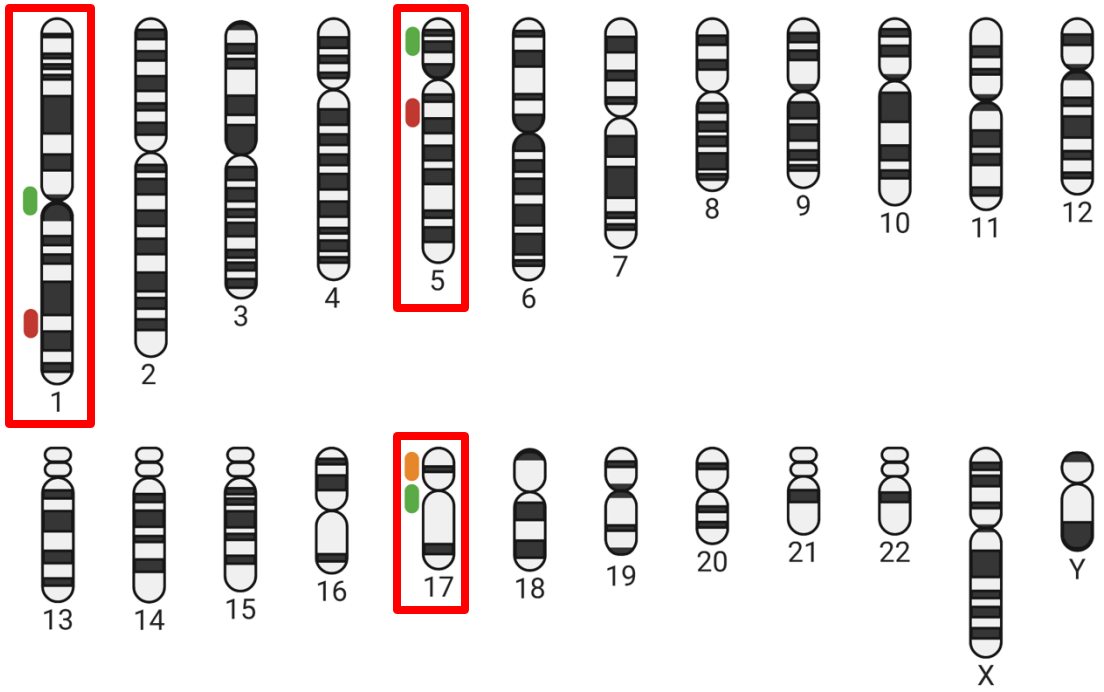
Abdellatif et al., 2018 , Pamukcuoglu et al., 2017.

Levels fluctuate with treatment

Other risk factors need to be considered

Cell Biology



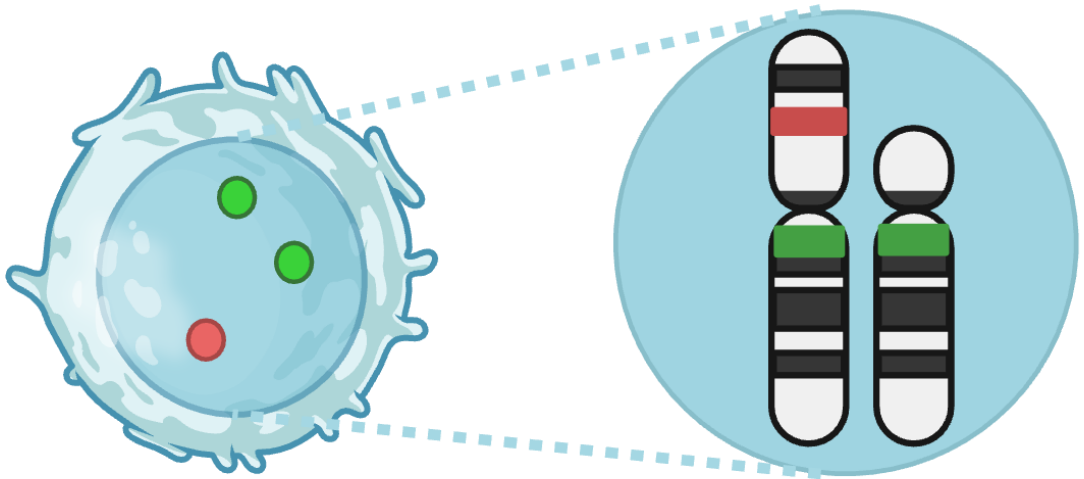


DNA

- Chromosomal abnormalities observed in 80% of transformed AML patients
- High-risk abnormalities;
  - Extra copy of a portion of chromosome 1 → **gain(1q)**
  - Loss of a portion of chromosome 5 → **del(5q)**
  - Loss of a portion of chromosome 17 → **del(17p)**
- Current testing requires bone marrow samples

Testing is not routine – if done, at MF diagnosis	**Bone marrow sampling is not suitable for monitoring**	**Bone marrow fibrosis makes testing difficult**

Can we detect chromosomal defects in progenitor cells?



CD34+ cell **del(17p)**

Detecting Disease Progression: New and Improved Method

1 tube of blood

Higher sensitivity

Predict progression earlier
→ timely intervention & improved patient outcomes

“Immuno-flowFISH”

- Automated method to assess chromosomes in single cells
- ***Immuno***: Immunophenotype (cell identity)
- ***Flow***: Flow cytometry principles (with digital cameras)
- ***FISH***: Chromosome assessment

Specific
Assess chromosomes in immunophenotyped cells

Sensitive (10^{-5})
Hundreds of thousands of cells analysed

Qualitative & Quantitative
Digital cameras and analysis software

Importantly – testing blood

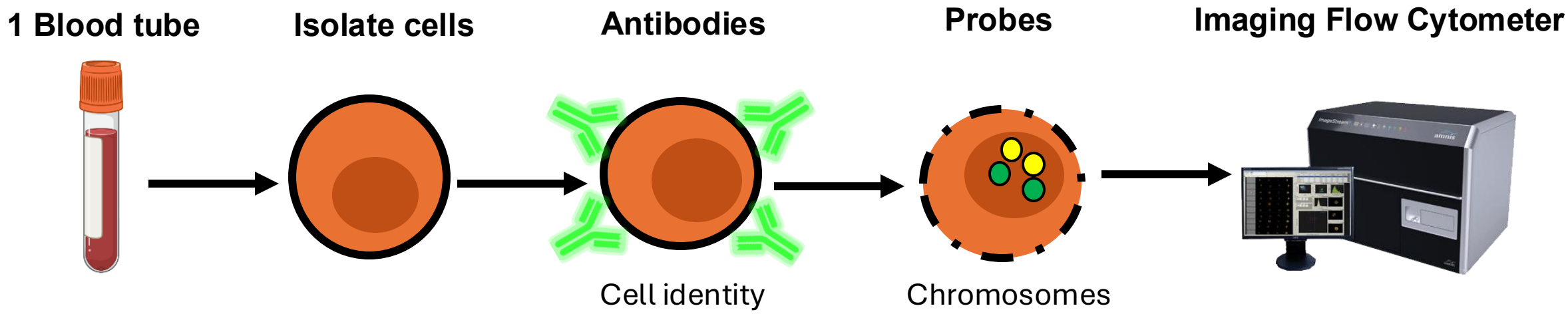
MPN Immuno-flowFISH Study Aims

Overall Aim

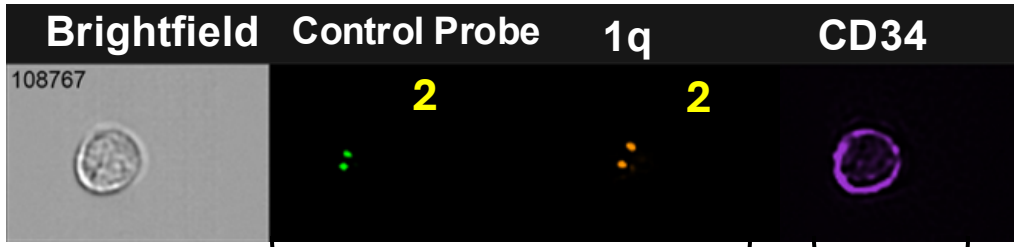
Assess chromosomal abnormalities in CD34+ cells and identify changes in clonal burden which may predict disease progression

Our translational research project is active and recruiting participants and collecting samples from consenting patients at Royal Perth, Fiona Stanley, Rockingham and Sir Charles Gairdner Hospitals

“Immuno-flowFISH” imaging flow cytometry method



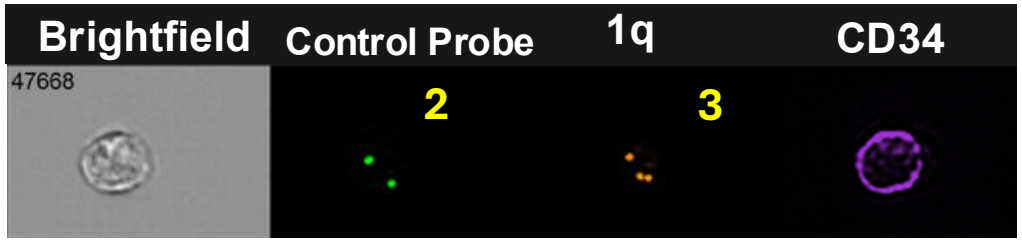
Normal
(2 spots)



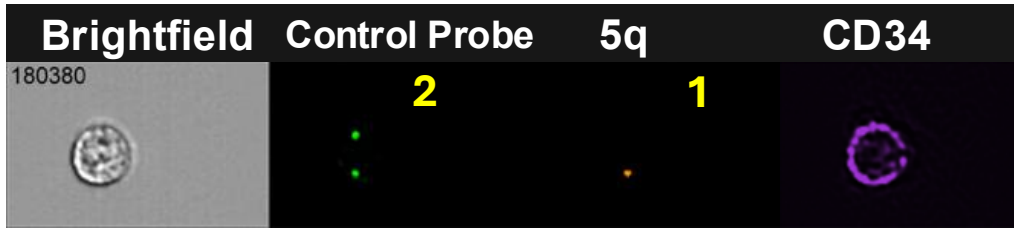
Chromosome

Immunophenotype (cell identity)

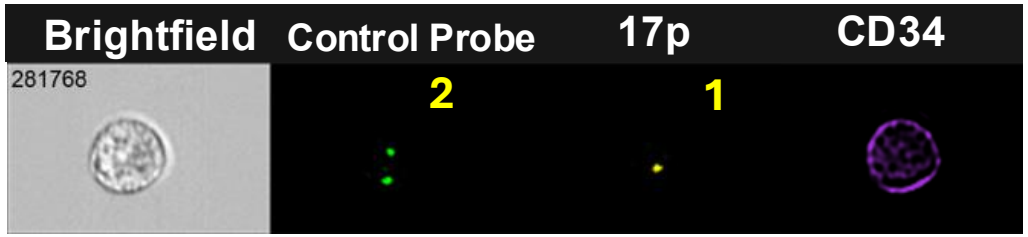
gain(1q)
(3 spots)



del(5q)
(1 spot)



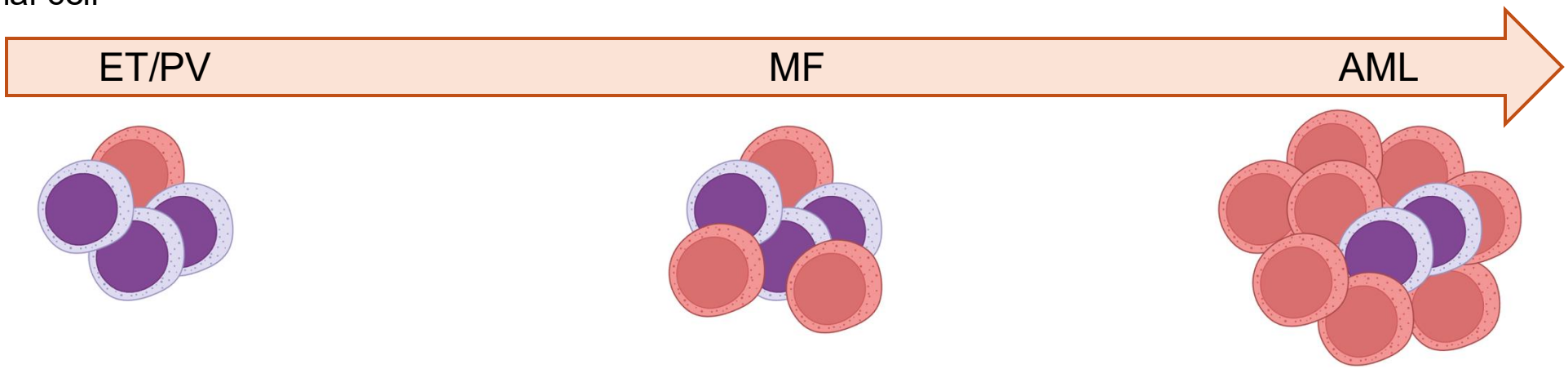
del(17p)
(1 spot)



Serial Monitoring

healthy cell

abnormal cell



- Monitoring patients → see dynamic changes in clonal burden
- As patients progress → rise in levels of CD34+ cells with a chromosomal abnormality

Is an abnormality present?

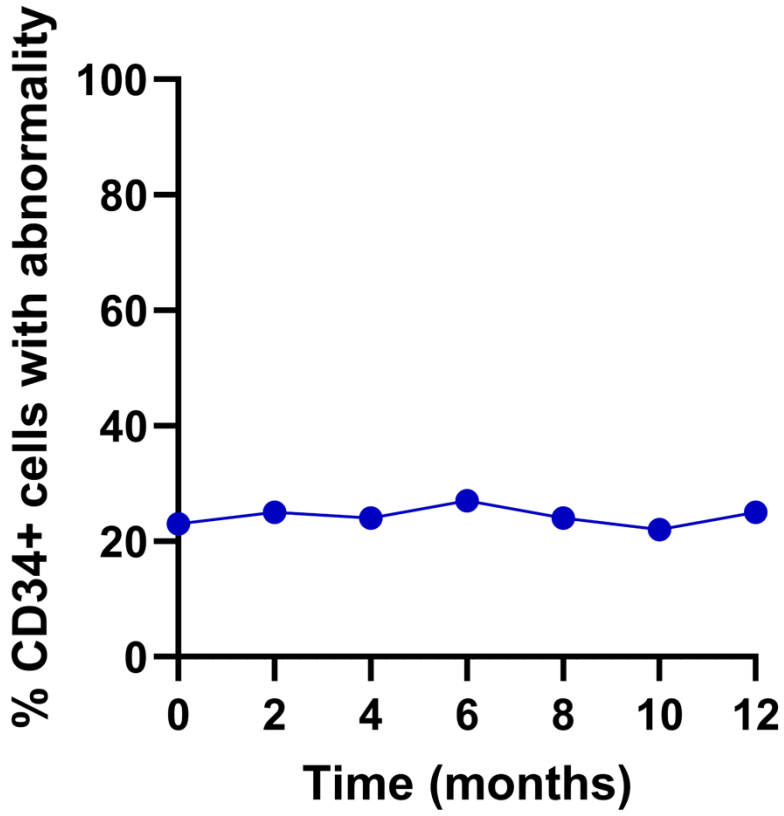
How many cells have it?

How is this changing over time?

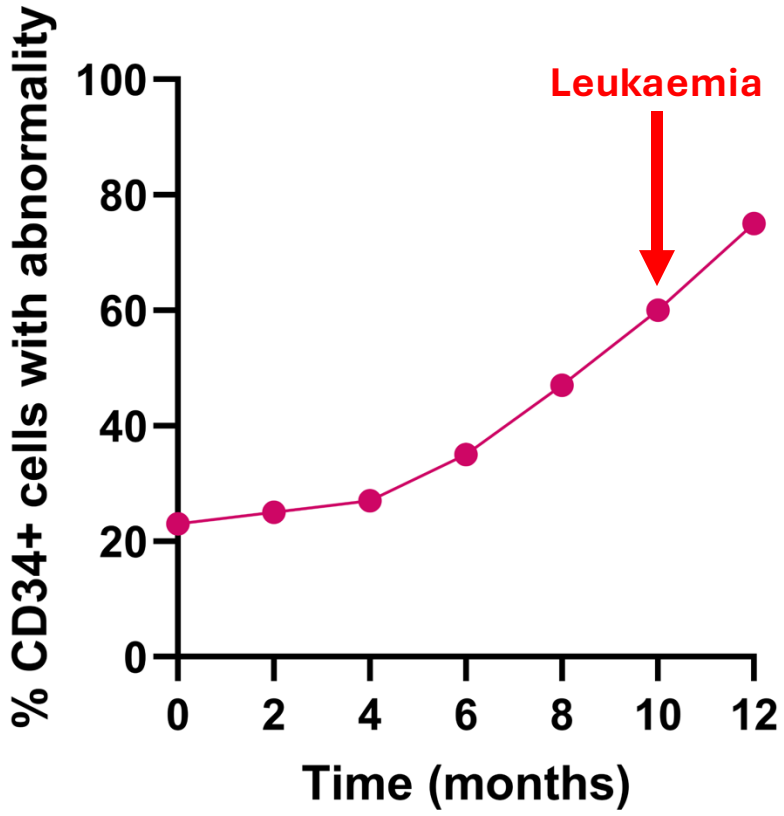
Can we detect it earlier?

Serial Monitoring

Chronic Disease
Stable burden



Progressing Disease
Increasing burden



Outcomes and Impact

Blood-based Monitoring Tool

More feasible for routine monitoring

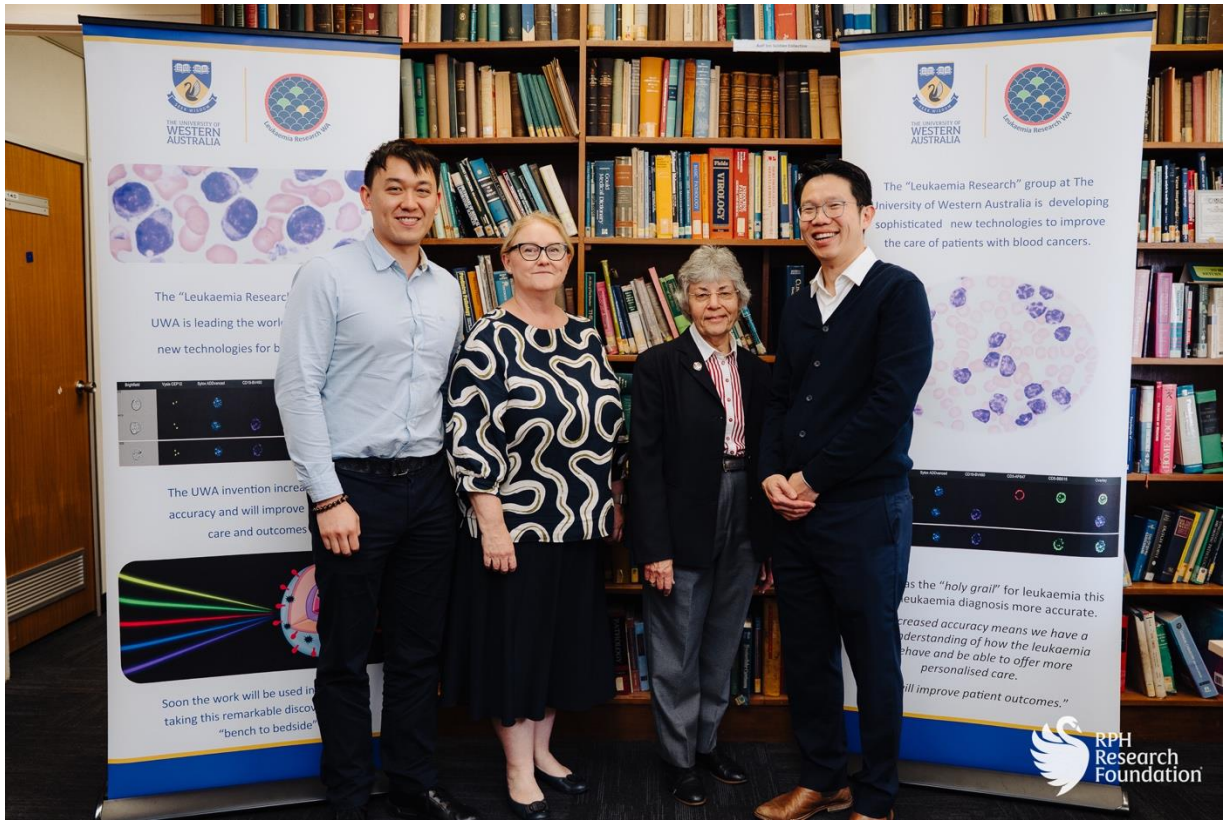
Early Identification

More sensitive than current methods and makes early intervention possible

Improved Management

Assist clinicians with treatment decisions and patient management

Predict leukaemia and improve patient outcomes


The "Leukaemia Research" group at The University of Western Australia is developing sophisticated new technologies to improve the care of patients with blood cancers.
RPH Research Foundation


RPH Research Foundation

Acknowledgements

All the patients and their families

University of Western Australia
Ryan Collinson
Lynne Wilson
Daria Buic
Naomi Damstra
Sarah Daly
Sarah Clarke
Andrea Aluner
Ann Wang
Henry Hui
Matthew Linden
Kathy Fuller
Belinda Guo
Wendy Erber

Department of Health WA
Zi Yun Ng
Hun Chuah
Marie O'Loughlin
Rachel Mynott
Phoebe Lee
RPH Haematology & Hospital Staff
FSH Haematology & Hospital Staff
RGH Haematology & Hospital Staff
SCGH Haematology & Hospital Staff

Community Representatives
Jane Fair

Contact:
ruby.hamilton@research.uwa.edu.au
tcpl-sbms@uwa.edu.au

Richard Walter Gibbon Medical Research Scholarship (UWA)
LT Thean and KC Yong Memorial Medical Research Top-up Scholarship
Research Training Program Domestic Fees Offset Scholarship