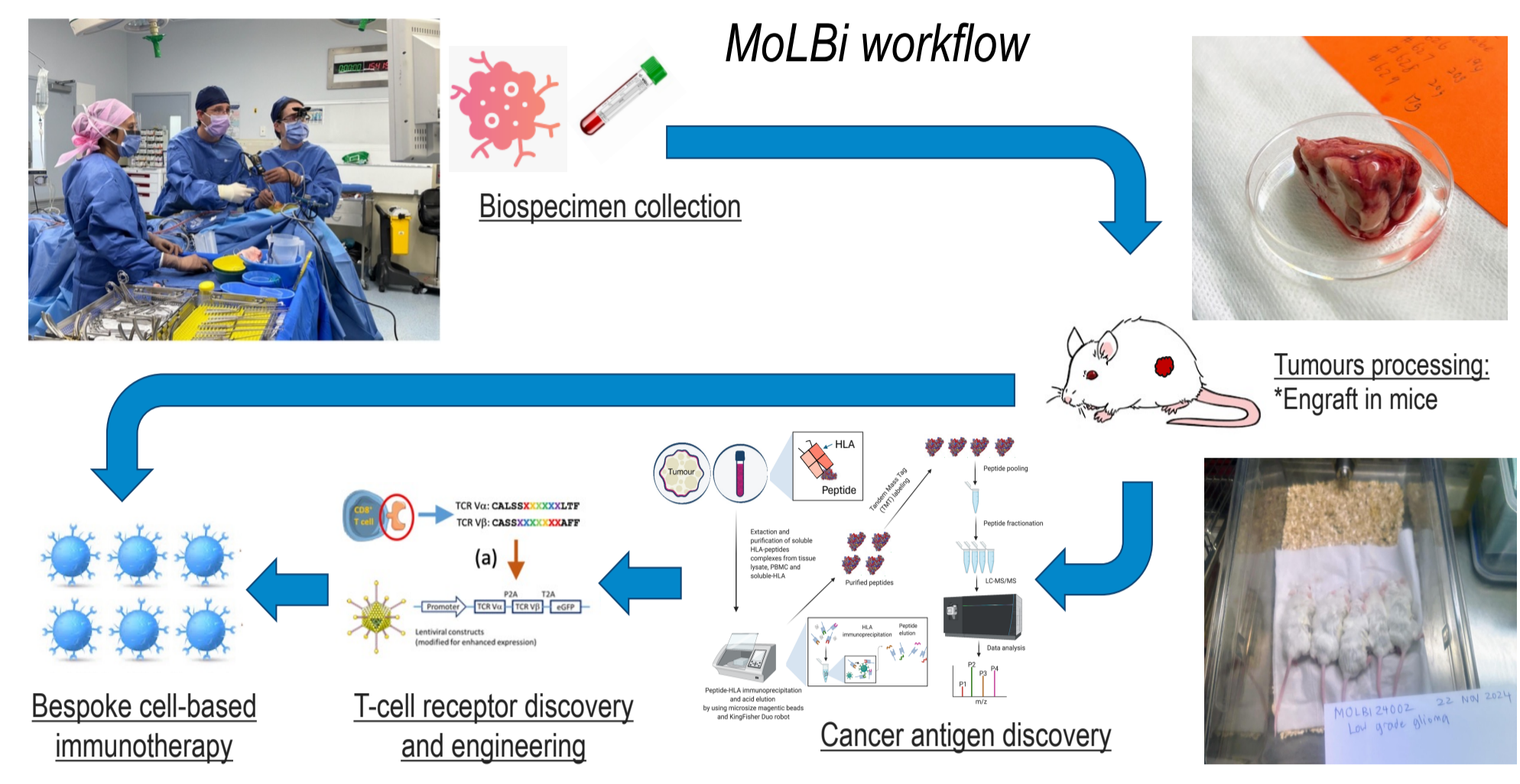


MoLBI: From Theatre to Therapy - Building Australia's First Live-Biobanking Platform for Precision Immunotherapy

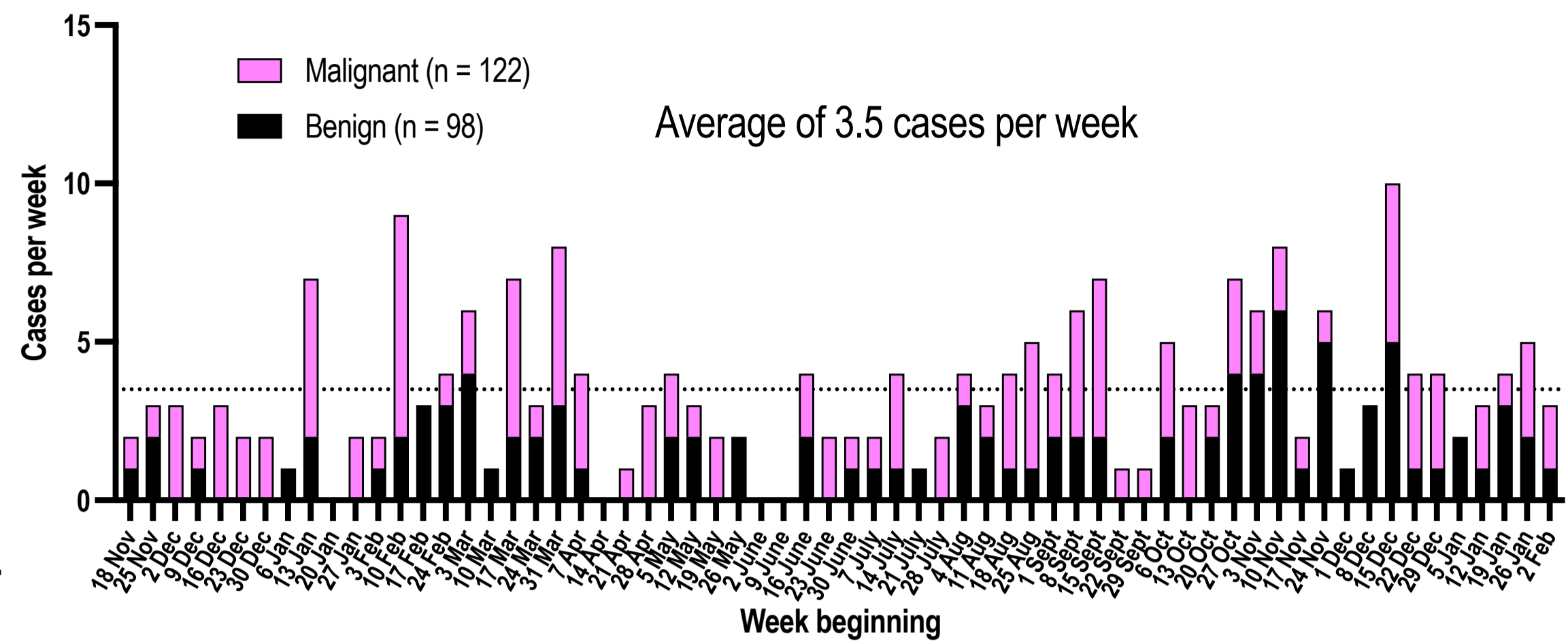
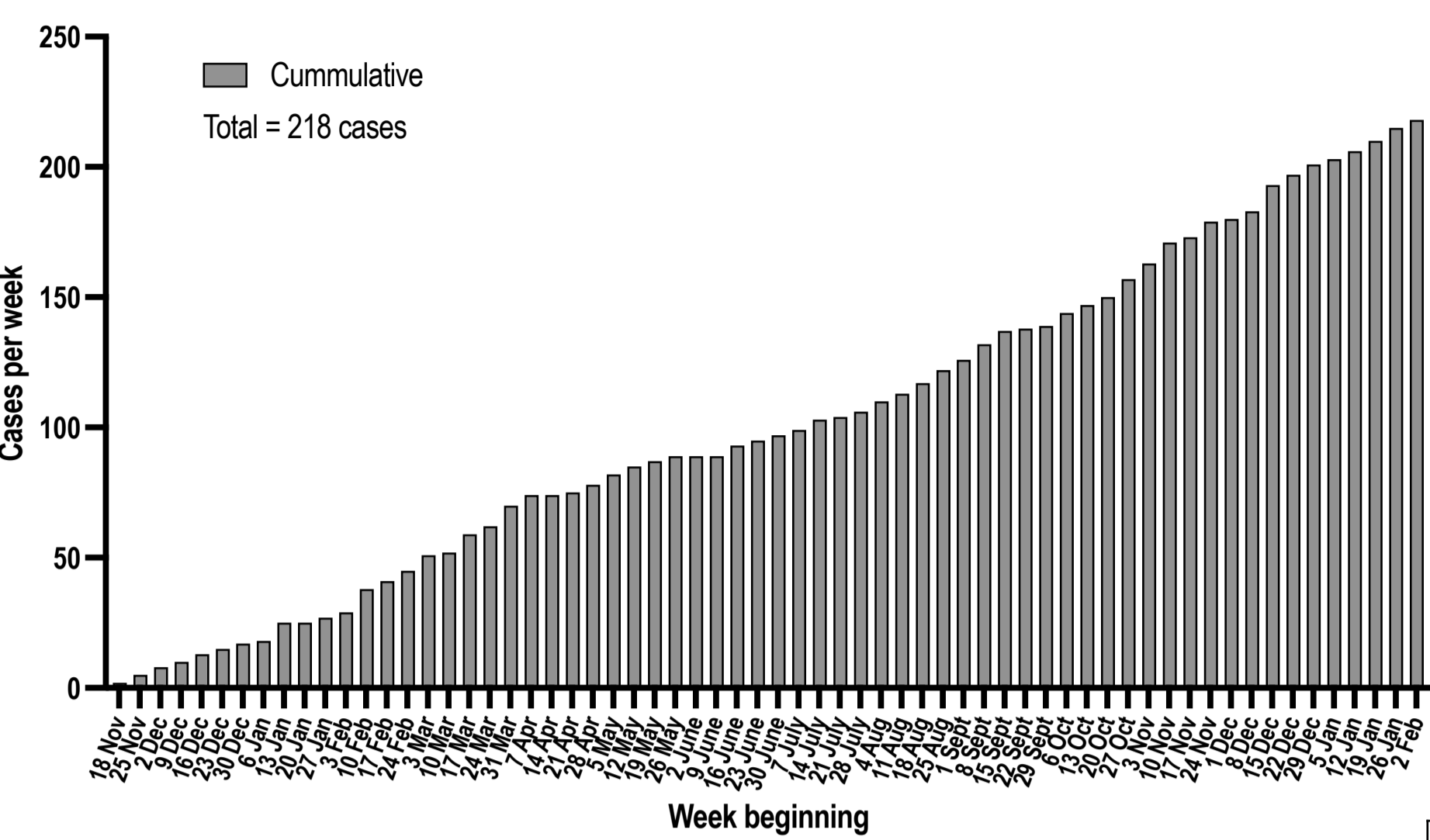
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Introduction: Most solid tumours, particularly brain, ovarian, pancreatic and upper gastrointestinal cancers, are immunologically “cold,” resistant to current immunotherapies, and with limited effective systemic options. Addressing this unmet need requires real-time access to fresh human tumours, high-resolution molecular profiling, and scalable preclinical models. To meet this challenge, we established the Monash Live-Biobanking (MoLBI) platform, a clinician-led initiative linking surgical theatres at Monash Health with cutting-edge laboratory pipelines at Monash University, supported by the Monash Health Oncology Department Research Support Program.



Rapid recruitment of a diverse brain tumour cohort with longitudinal paired sampling.



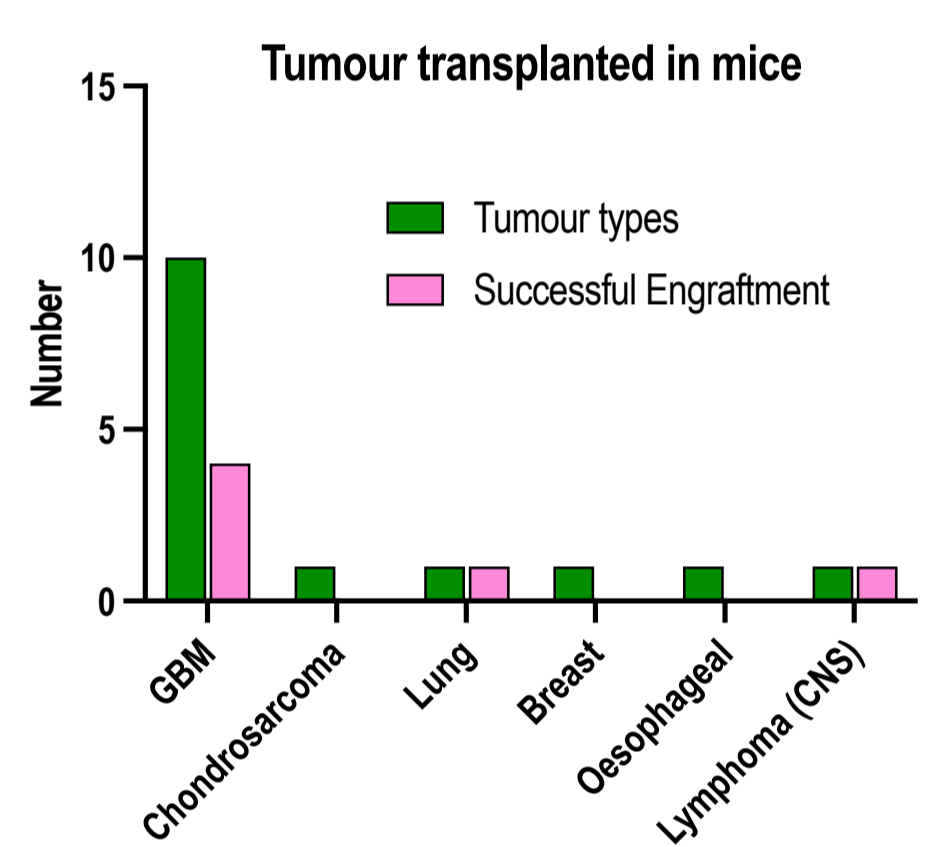
Since its launch in November 2024, the Monash Live Biobanking (MoLBI) platform has sustained a high recruitment rate of approximately 3.5 patients per week. To date, over 218 patients have been enrolled, with 223 fresh tumour biospecimens collected across a diverse range of primary and secondary brain tumours. Five patients contributed paired tumour specimens from separate surgical episodes, enabling longitudinal within-patient analyses. These paired cases span both primary and secondary tumours and include transitions in histopathological grade and clinical context, underscoring the platform's capacity to support dynamic translational and Phase Zero studies.

| MoLBI ID | Diagnosis | Paired sampling interval | Key feature |
|------------|---------------------------------|--|--|
| MOLBI24002 | Oligodendroglioma (IDH-mut, G2) | Initial resection and interval repeat surgery | Longitudinal sampling of low-grade glioma |
| MOLBI24015 | Ependyoma | Emergency resection followed by elective surgery | Change in clinical context and tumour behaviour |
| MOLBI24057 | Metastatic lung adenocarcinoma | Elective surgery followed by emergency resection | Longitudinal metastatic disease sampling |
| MOLBI24106 | Glioblastoma (IDH-wild type) | Emergency resection followed by elective surgery | Treatment-associated tumour evolution |
| MOLBI24145 | High-grade glioma | Two emergency resections | Aggressive disease course with rapid progression |

Patient Demographics:

The MoLBI cohort includes 218 patients (median age 59.6 years; range 19–88) with equal sex distribution, predominantly primary brain tumours (83%) spanning benign, malignant, and metastatic disease. The GBM subgroup comprises 65 patients (median age 63.8 years) with a strong male predominance (71%), with almost all cases representing primary glioblastoma (97%).

| Characteristic | Value |
|---------------------------|--------------|
| Total patients, n | 218 |
| Median age, years (range) | 59.6 (19–88) |
| Female sex, n (%) | 109 (50.0) |
| Male sex, n (%) | 109 (50.0) |
| Primary tumours, n (%) | 181 (83.0) |
| Secondary tumours, n (%) | 37 (17.0) |
| Benign tumours, n (%) | 113 (51.8) |
| Malignant tumours, n (%) | 75 (34.4) |
| Metastatic tumours, n (%) | 30 (13.8) |



Overall patient demographics

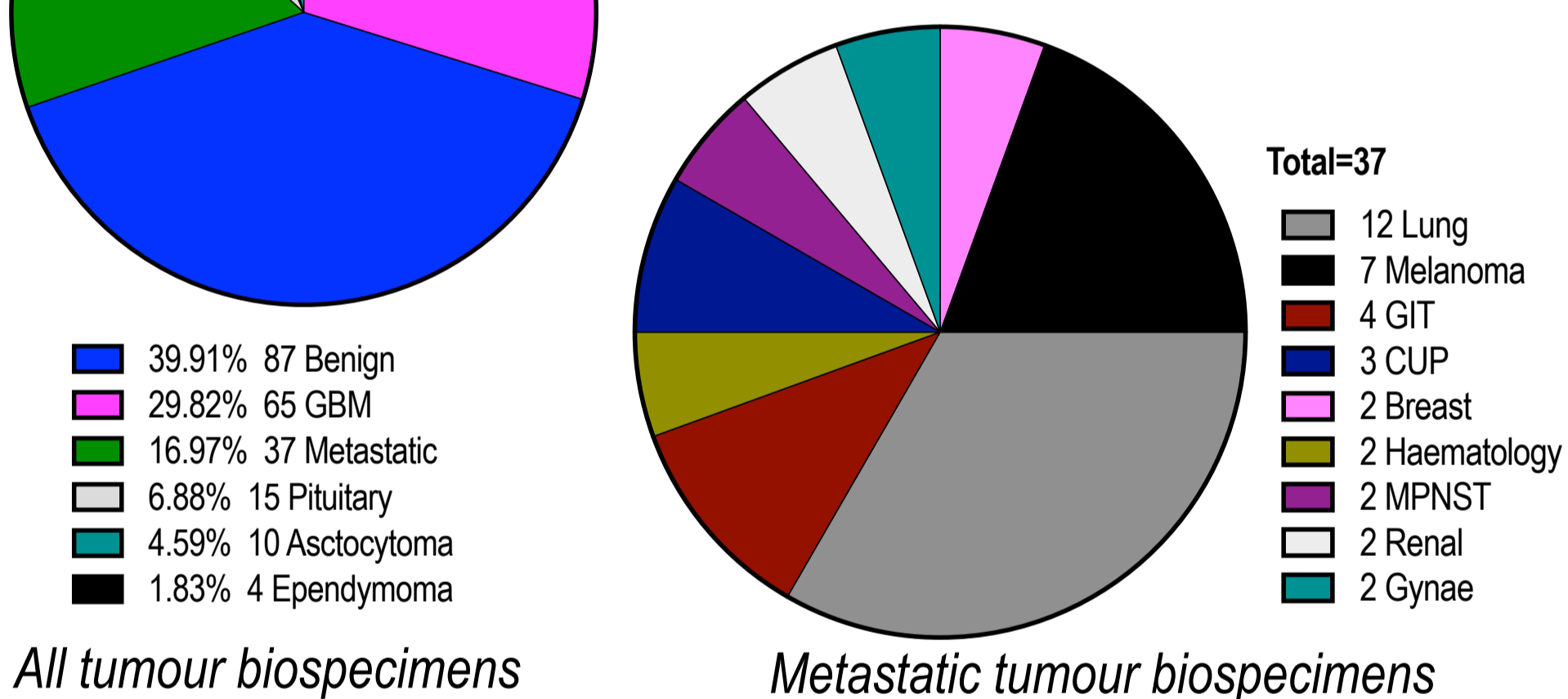
| Characteristic | Value |
|---------------------------|--------------|
| Total GBM patients, n | 65 |
| Median age, years (range) | 63.8 (24–88) |
| Female sex, n (%) | 19 (29.2) |
| Male sex, n (%) | 46 (70.8) |
| Primary GBM, n (%) | 63 (96.9) |
| Secondary GBM, n (%) | 2 (3.1) |

GBM patient demographics

Patient-derived xenograft (PDX) models have been successfully established from a subset of MoLBI tumours, enabling in vivo functional validation and therapeutic testing. These models provide a biologically faithful platform to study tumour behaviour and treatment response, complementing the multi-omic analyses generated from matched patient biospecimens.

Broad Tumour Spectrum Captured:

The MoLBI biobank encompasses a diverse range of brain tumour types, spanning benign, malignant, and metastatic disease, and reflecting real-world neurosurgical practice. High-grade gliomas represent a major proportion of the cohort, alongside lower-grade gliomas, meningiomas, pituitary tumours, schwannomas, and brain metastases. This diagnostic breadth underpins the platform's versatility for discovery biology, translational studies, and therapy development across multiple tumour contexts.

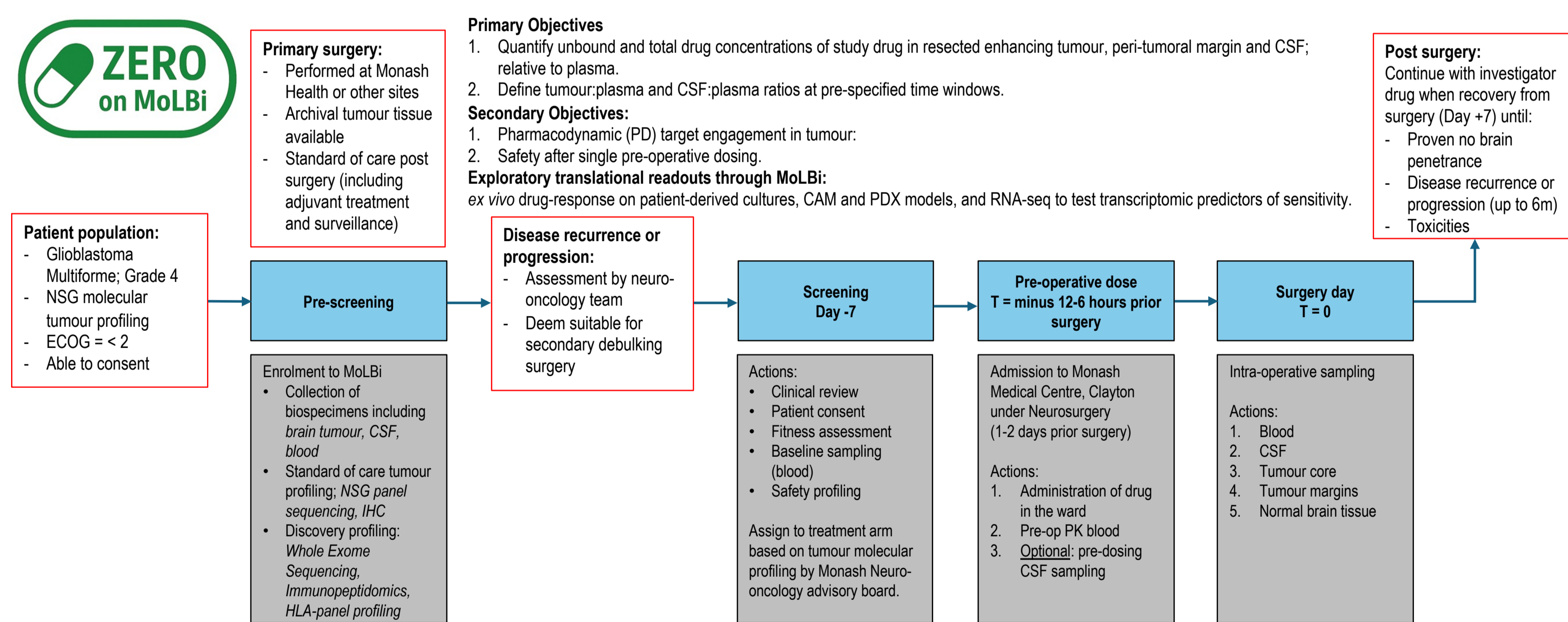


Bespoke TCR Discovery from a Recurrent GBM Patient Using Single-Cell Profiling and Immunopeptidomics

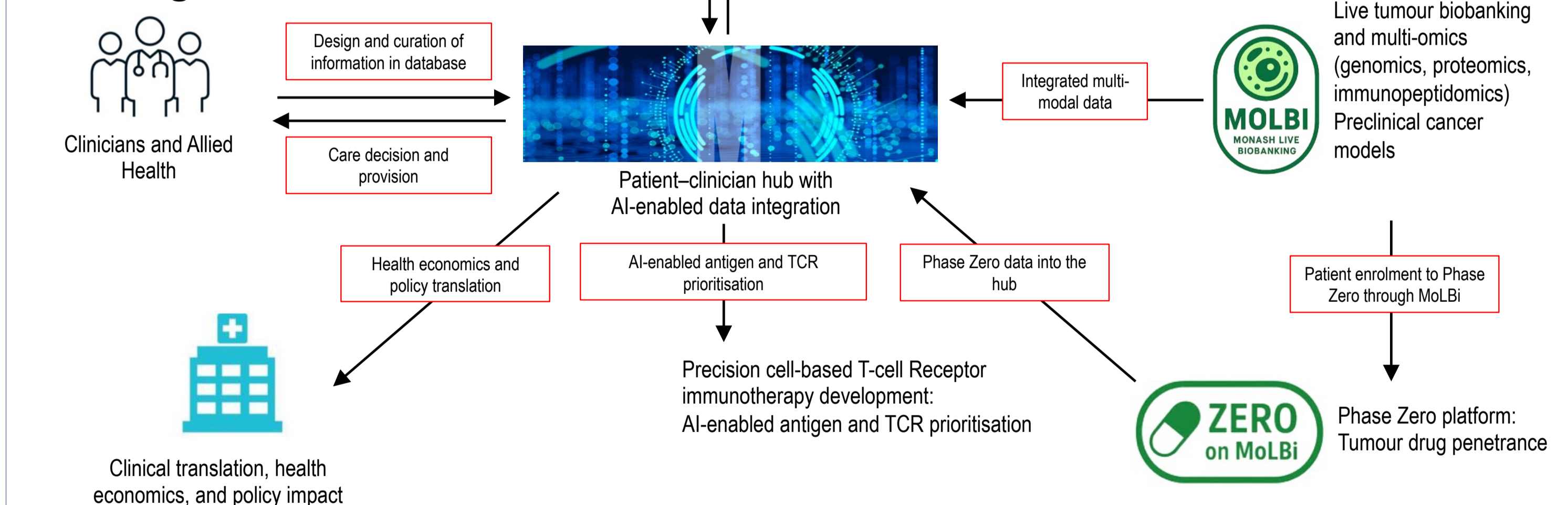
Tumour tissue from the recurrent glioblastoma patient MoLBI24087 was analysed using single-cell RNA sequencing integrated with immunopeptidomics, enabling the identification of four tumour-specific antigens (A–D) uniquely expressed and presented by the cancer. Candidate peptides were prioritised for functional validation and used to stimulate HLA-matched CD8 T cells via dendritic cell co-culture, supporting antigen-specific T-cell expansion and TCR discovery. This case demonstrates MoLBI's capacity to translate patient-derived tumour material into bespoke T-cell receptor therapeutics for personalised immunotherapy.

MoLBI-Enabled Phase Zero Platform Study for Rapid Translational Decision-Making

The MoLBI platform underpins a first-in-human Phase Zero, adaptive platform study at Monash, designed to generate early, decision-critical data on drug delivery, target engagement, and tumour pharmacodynamics in patients undergoing neurosurgical resection. Leveraging MoLBI's established intra-operative biospecimen collection and multi-omic profiling workflows, the study integrates pre-operative micro-dosing with comprehensive sampling of blood, cerebrospinal fluid, tumour core and margins at surgery. This industry-funded program, co-designed with consumers from Brain Tumour Alliance Australia (BTAA), will commence recruitment in mid-2026 and provides a scalable framework to rapidly de-risk and prioritise novel therapies for downstream clinical development.



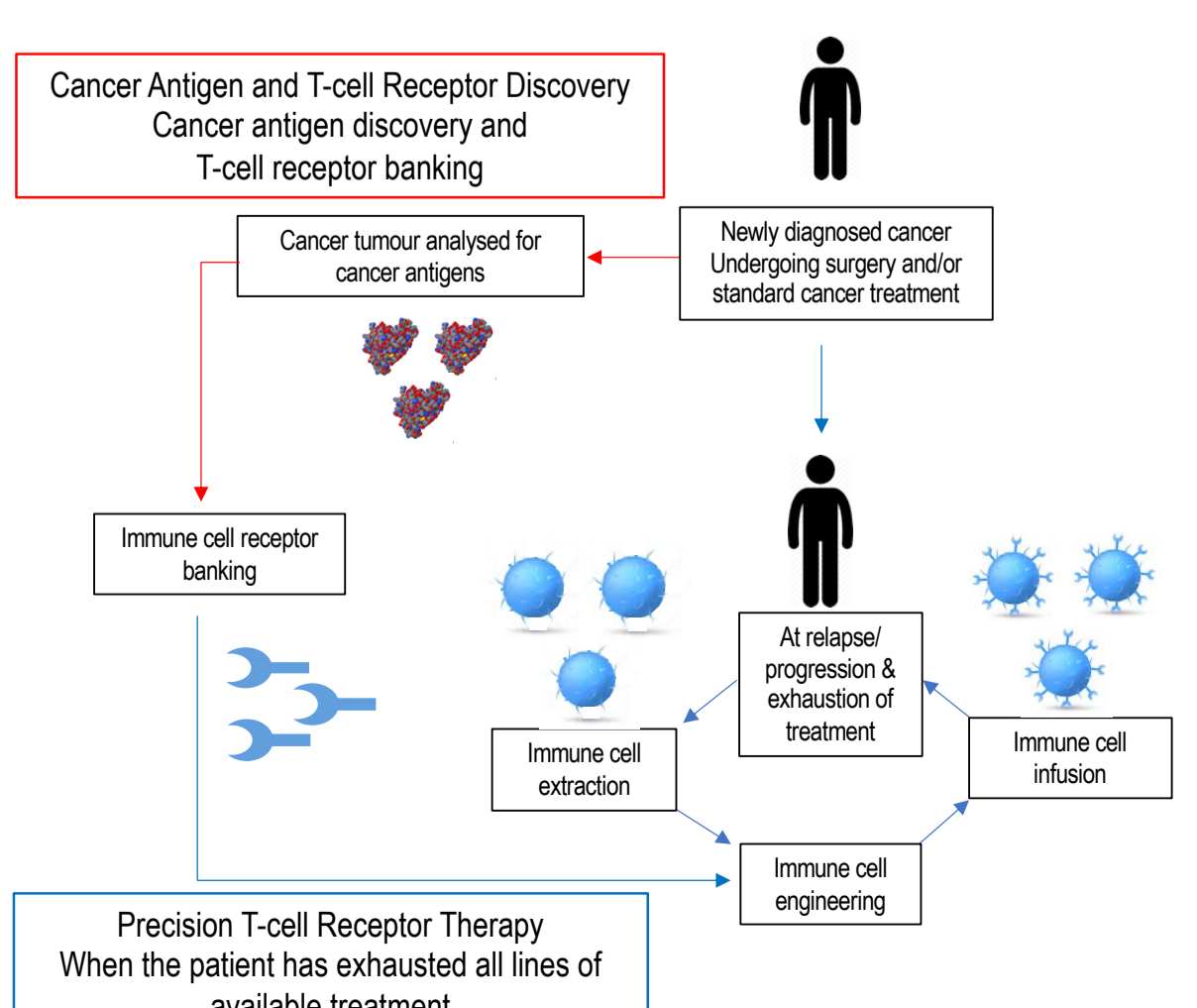
AI-Enabled Integration of Patient- and Carer-Reported Outcomes with Multi-Omic Tumour Profiling



The next phase of MoLBI will leverage AI and machine learning in partnership with the Monash Faculty of Information Technology (Prof Enes Makalic) to capture longitudinal patient- and carer-reported outcomes and integrate these data with tumour genomics and immunopeptidomics. This unified, multi-modal data infrastructure will enable rapid antigen prioritisation and TCR discovery, linking real-world patient experience with biological insight. By embedding AI-driven analytics within the MoLBI and Phase Zero ecosystem, this approach aims to accelerate the translation and deployment of bespoke TCR-based therapies.

Building a Longitudinal Pipeline for Bespoke T-Cell Therapies

MoLBI aims to establish a longitudinal, patient-centred pipeline that captures tumour and immune information from diagnosis through disease progression to enable early immune receptor banking and T-cell receptor discovery. This integrated framework positions patients for bespoke T-cell therapies at relapse or treatment exhaustion, embedding personalised immunotherapy into routine cancer care.



Summary and future plans:

- A living biobank at scale: MoLBI rapidly captures fresh tumours and longitudinal samples, creating a continuously growing, real-world resource embedded in routine neurosurgical care.
- From biology to therapy: Deep multi-omic and functional profiling enables direct translation from patient tumours to bespoke T-cell receptor discovery.
- Early clinical decision-making: An industry-funded, adaptive Phase Zero platform will generate critical data to prioritise and de-risk novel therapies.
- The future of personalised immunotherapy: AI-enabled integration of patient-reported outcomes with tumour biology will accelerate truly personalised, scalable T-cell therapies.

