

Bridging Expert-Led Spatial-Multimodal Omics Analysis and AI Integration in the POETIC Breast Cancer Trial (NCT02338310)

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BACKGROUND

Large-scale clinical trials such as POETIC (NCT02338310; $n \approx 4,000$ patients with >8,000 paired pre- and post-treatment tumour samples) generate complex datasets spanning clinical, molecular, and spatial modalities. The POETIC trial, which evaluated peri-operative endocrine therapy in hormone receptor-positive early breast cancer, represents one of the most data-rich translational resources in the UK, combining detailed clinicopathological annotations with extensive multi-omics profiling. Molecular datasets encompass bulk RNA sequencing, targeted mutational profiling, quantitative proteomics, multiplex immunofluorescence, digitised haematoxylin and eosin (H&E) and Ki67 immunohistochemical (IHC) stains, and spatially resolved transcriptomic and proteomic profiles generated using NanoString GeoMx Digital Spatial Profiling.

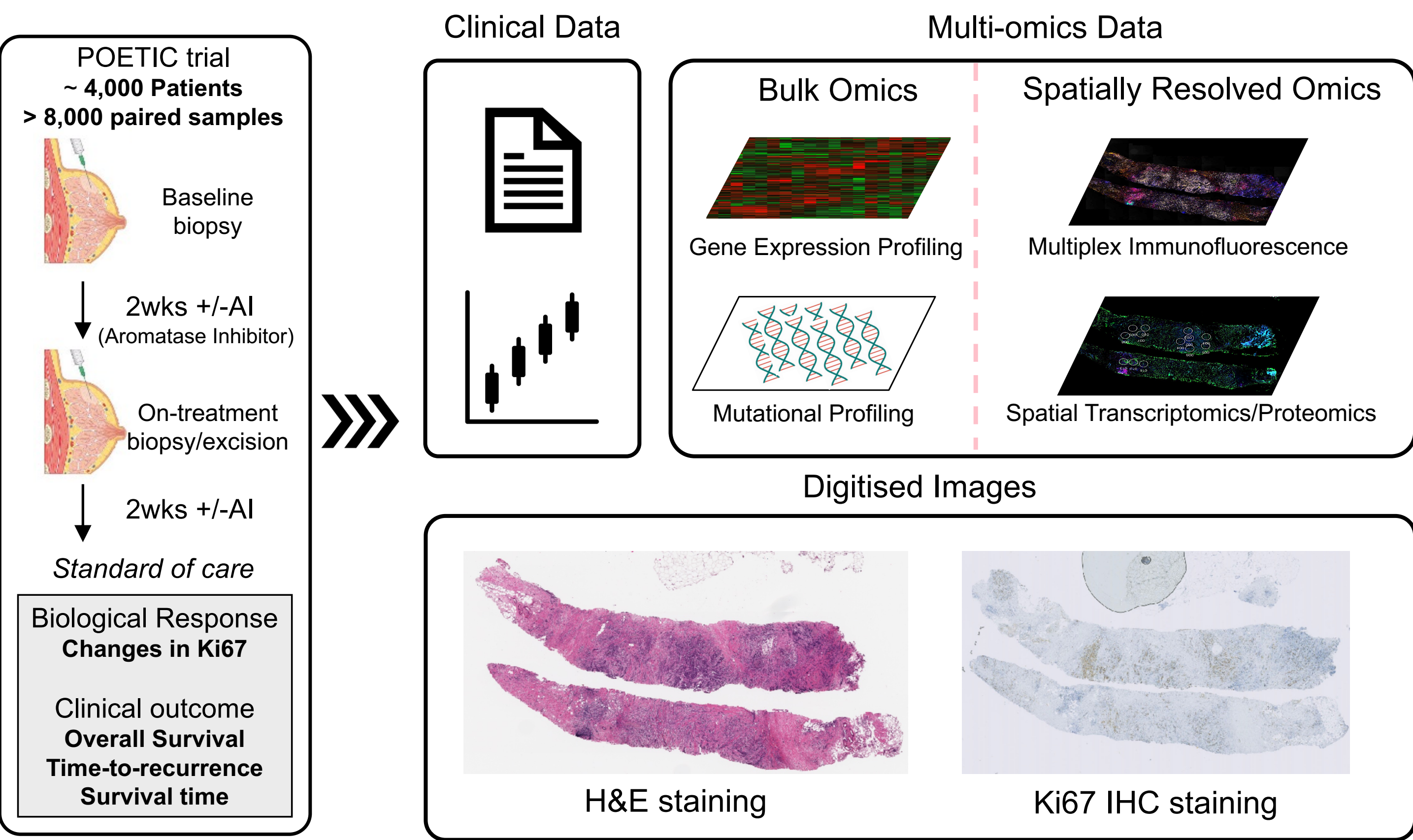


Figure 1 POETIC trial and its data modalities.

POETIC-AI Platform as a Multimodal Integration Strategy

To harness this multidimensional complexity, we developed *POETIC-AI* using a commercial software component as an interim technical solution. It is an AI-enabled integration and analytics platform that unifies clinical records, molecular assays, and analytical outputs within a secure, version-controlled, and interoperable network.

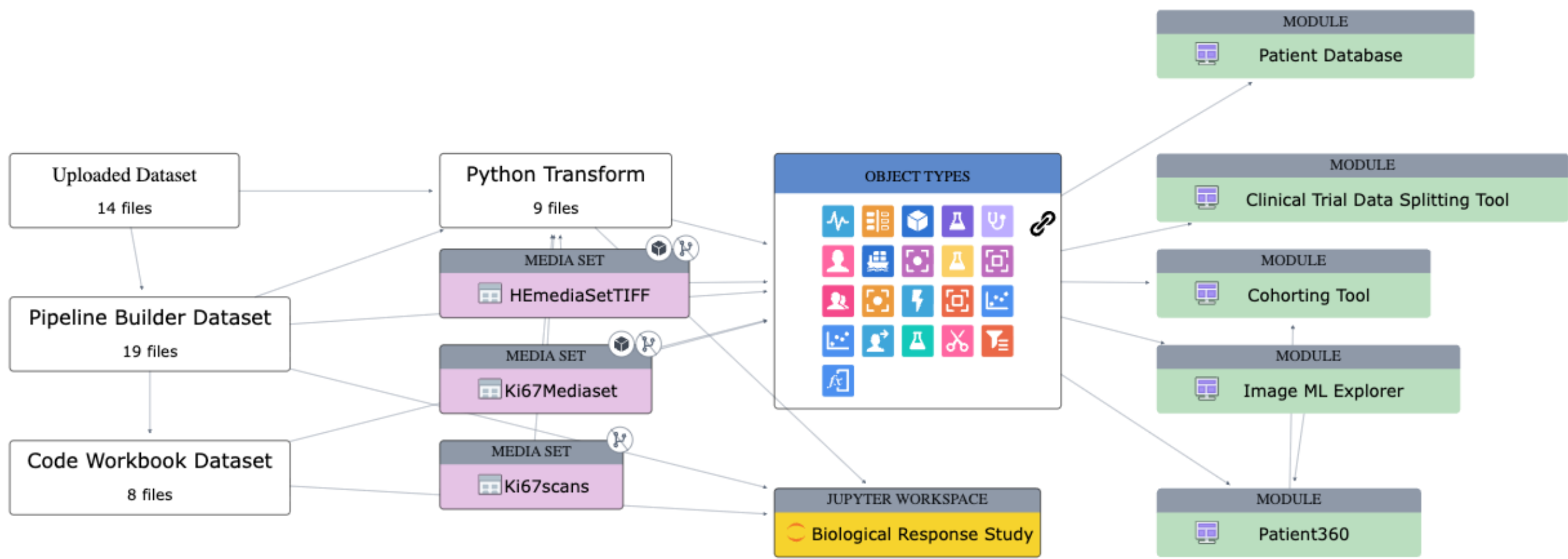


Figure 2 The ontology network in the *POETIC-AI* platform.

The platform is built on a graph-based ontology, mapping relationships among entities such as patient, sample, assay, and derived molecular features. This architecture supports dynamic data linkage, hierarchical querying, and real-time visualisation of multimodal relationships. At patient level, the ontology allows us to visualise and access all relevant datasets linked to an individual patient. This structure enables efficient querying and supports rapid retrieval of multimodal patient-level information.

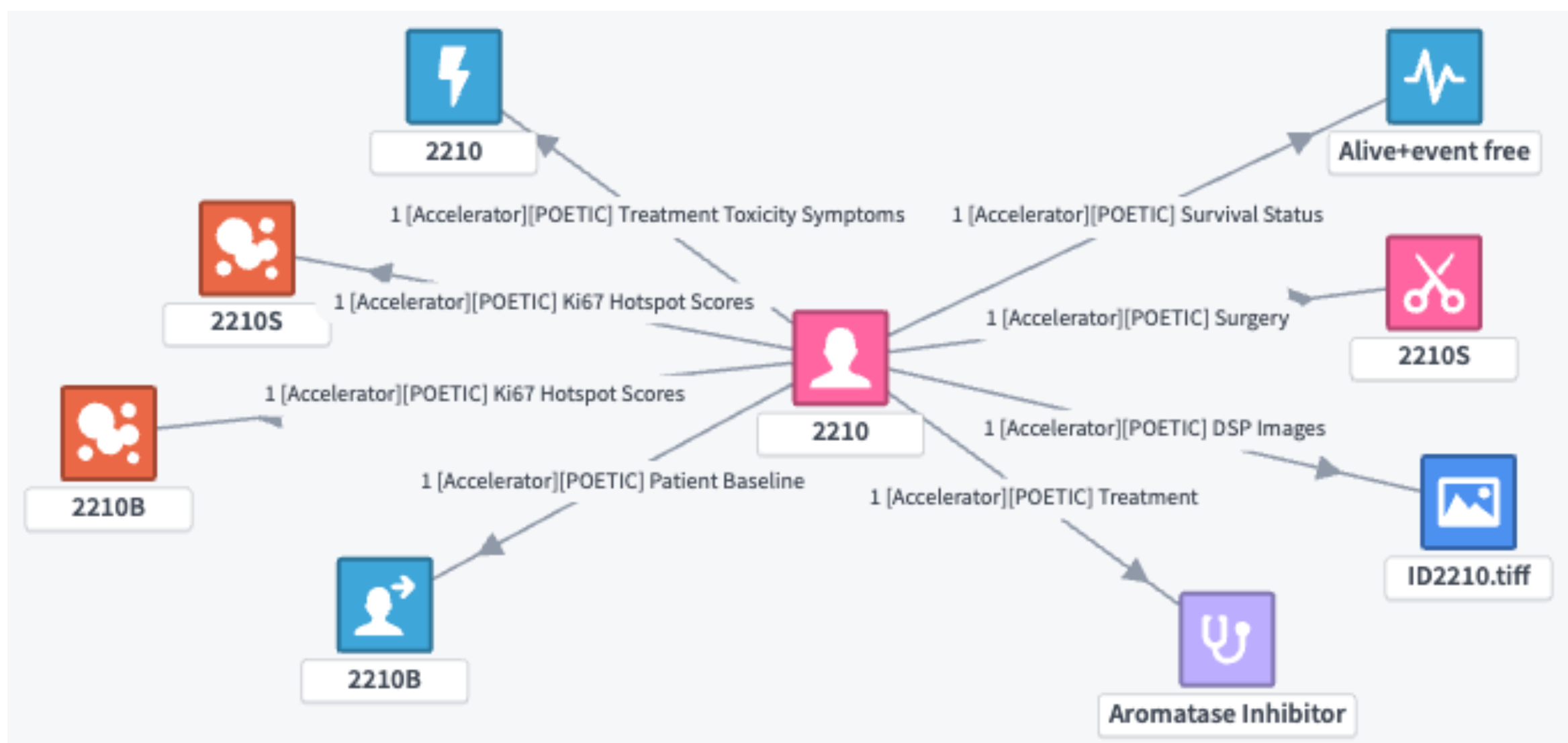


Figure 3 The patient-level ontology network in the *POETIC-AI* platform.

POETIC-AI Enabled Applications and Large-Language Model Interface

We have developed a series of graphical applications within *POETIC-AI* to support visualisation, exploration and analysis of the multimodal data from POETIC. Moreover, integrated large language model-based natural-language interface enables users to interrogate the dataset using contextual queries. These applications allow accessible analysis without the need of extensive computational skills.

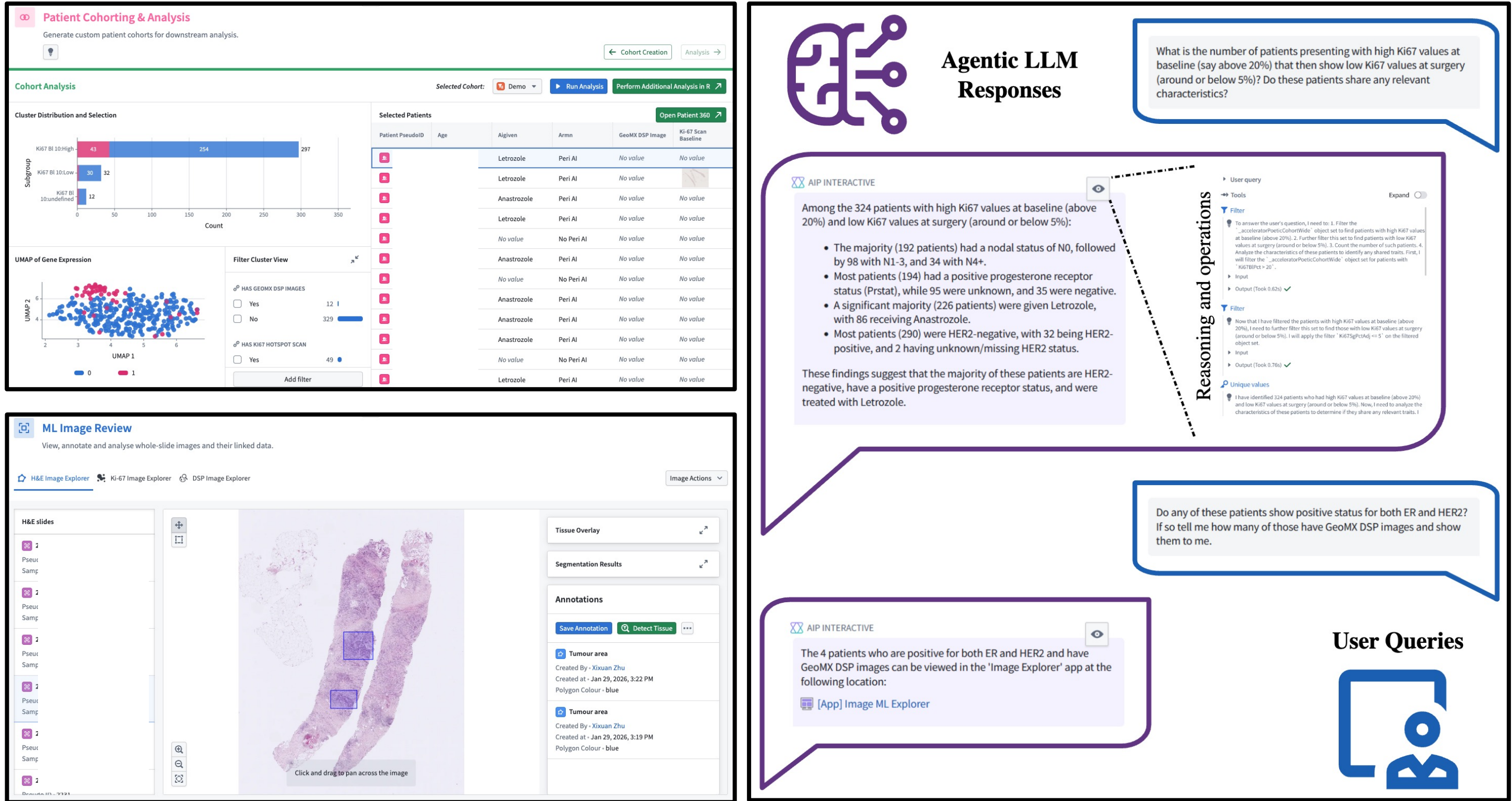


Figure 4 *POETIC-AI* enabled applications and large-language model interface.

POETIC-AI Facilitates Spatial Omics Visualisation and Analysis

Expert-led spatial omics analyses focused on tumours with divergent endocrine therapy responses, enabling high-resolution interrogation of intra-tumoral architecture, immune microenvironments, and spatially restricted signalling. Manual and statistical analyses revealed increased spatial heterogeneity and disrupted proliferative signalling in resistant tumours.

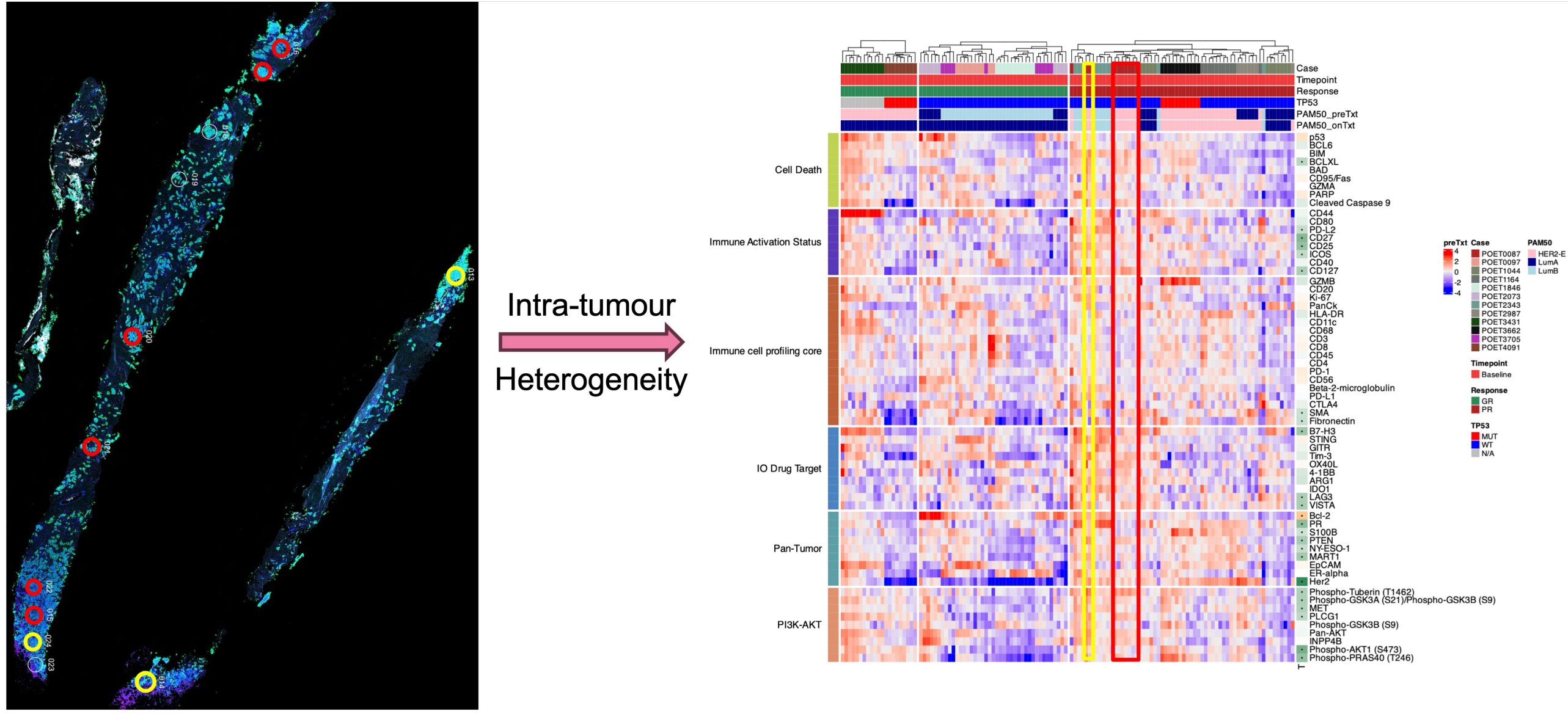


Figure 5 Expert-led spatial omics analysis to interrogate intra-tumoral architecture.

We extended the capability of the platform and developed our own spatial visualisation tool that overlays molecular signatures and expression gradients onto histologically annotated tissue regions. This enables interactive visual exploration of molecular-spatial correlations and sub-clonal diversity.

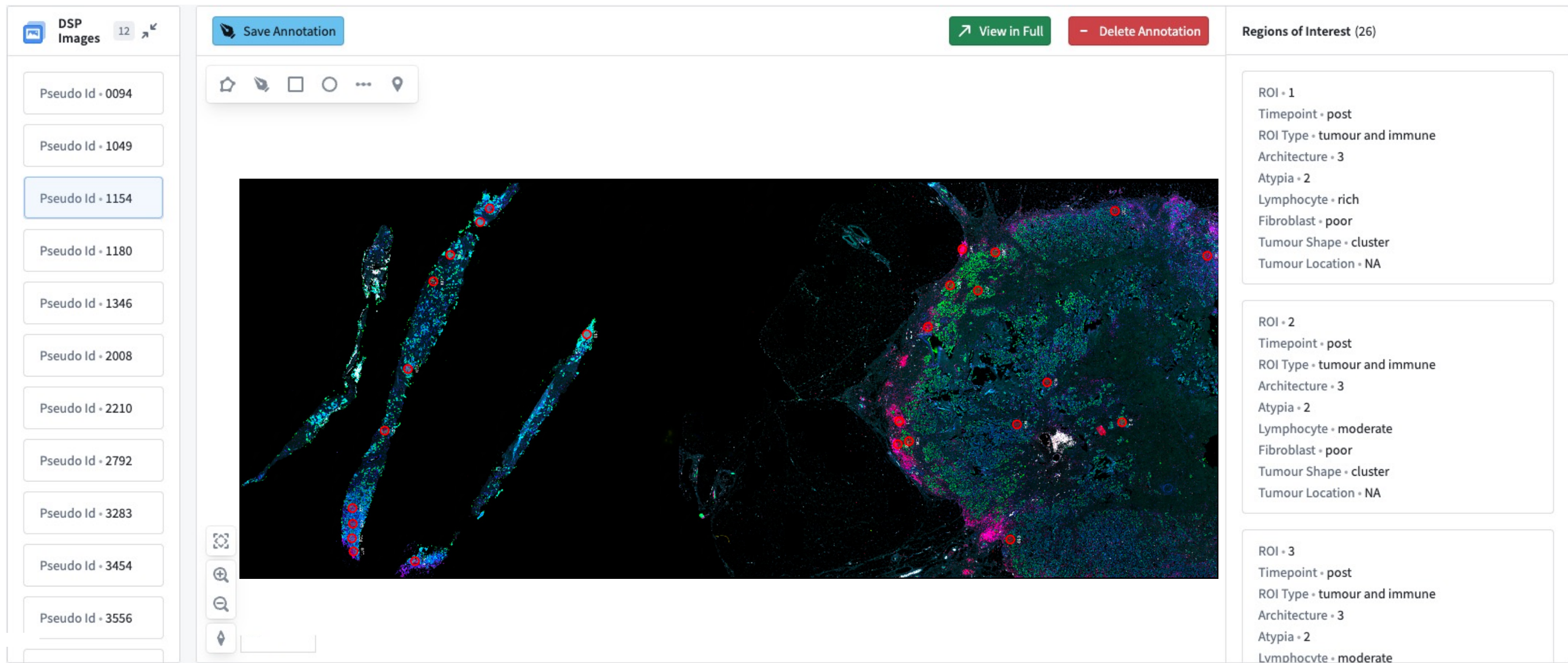


Figure 6 Spatial omics visualisation and analysis application.

CONCLUSIONS

The *POETIC-AI* framework provides a technically robust, extensible, and federated model for future translational ecosystems, accelerating biomarker discovery and data sharing, as well as supporting precision oncology in complex clinical trial settings.