

# Precision Medicine Through Multi-Omics Modeling

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## ABSTRACT

*Precision medicine aims to tailor therapeutic strategies to individual patients based on their unique molecular profiles, yet clinical implementation remains limited because single-omics data (genomics alone, transcriptomics alone) capture only one dimension of disease biology. Multi-omics integration -- combining genomics, transcriptomics, proteomics, metabolomics, and epigenomics -- promises comprehensive molecular characterisation that enables accurate patient stratification, treatment response prediction, and mechanism-based therapy selection. However, multi-omics datasets are high-dimensional (>100,000 combined features), heterogeneous (different data types, scales, missing patterns), and expensive to generate, creating fundamental computational and practical challenges. This study developed and benchmarked six multi-omics integration approaches -- single-omics baselines (genomics-only, transcriptomics-only), simple concatenation, Similarity Network Fusion (SNF), Multi-Omics Factor Analysis (MOFA+), autoencoder-based integration (OmiVAE), and a proposed Multi-Omics Precision Medicine Transformer (MOPMT) combining modality-specific tokenisation, cross-omics attention, missing-omics robustness, and interpretable pathway-level embeddings -- for three precision medicine tasks: cancer subtype classification (TCGA pan-cancer,  $n = 9,624$ , 33 cancer types, 5 omics layers), drug response prediction (GDSC + CCLE,  $n = 986$  cell lines, 198 drugs), and patient survival stratification (TCGA + METABRIC breast cancer,  $n = 3,842$ ). MOPMT achieved the highest accuracy across all tasks: cancer subtyping macro-F1 0.918 (vs best single-omics 0.762, concatenation 0.842, MOFA+ 0.872;  $p < 0.001$ ), drug response AUROC 0.846 (vs 0.724 genomics-only, 0.812 OmiVAE;  $p < 0.001$ ), and survival C-index 0.748 (vs 0.682 transcriptomics-only, 0.724 SNF;  $p < 0.001$ ). Critically, MOPMT maintained 92.4% of full-omics performance when any two of five omics layers were missing -- addressing the clinical reality that complete multi-omics profiling is rarely available. Cross-omics attention analysis revealed that proteomics contributed the most incremental value for drug response prediction (24.6% attention weight), while methylation dominated survival stratification (28.4%), providing omics-prioritisation guidance for cost-constrained clinical implementation.*

**Keywords:** Precision medicine; Multi-omics integration; Cancer subtyping; Drug response prediction; Transformer models; Patient stratification; Missing data robustness; Pathway analysis; Molecular profiling

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## 1. Introduction

The promise of precision medicine -- delivering the right treatment to the right patient at the right time -- has been a central aspiration of biomedical research since the completion of the Human Genome Project. Genomics-guided therapy has achieved notable successes: EGFR-targeted therapy in EGFR-mutant lung cancer, HER2-targeted therapy in HER2-amplified breast cancer, and BRAF inhibitors in BRAF-mutant melanoma collectively benefit millions of patients annually (Collins and Varmus, 2015). However, genomic variants alone explain only 10-30% of drug response variability, and single-gene biomarkers fail to capture the biological complexity driving most treatment decisions (Paananen and Fortino, 2020). The remaining variability is distributed across transcriptional programmes, protein abundance and modification states, metabolic rewiring, and epigenomic reprogramming -- information captured by complementary omics technologies.

### 1.1 The Multi-Omics Landscape

Five major omics layers provide complementary molecular information. Genomics (whole-exome/genome sequencing) identifies inherited and somatic mutations, copy number alterations, and structural variants -- the static genetic blueprint. Transcriptomics (RNA-seq) measures gene expression levels reflecting the dynamic transcriptional state. Proteomics (mass spectrometry, RPPA) quantifies protein abundance and post-translational modifications -- the functional effectors. Metabolomics (LC-MS/MS, NMR) captures the small-molecule metabolic phenotype reflecting pathway activity. Epigenomics (DNA methylation arrays, ATAC-seq) measures chromatin accessibility and methylation states that regulate gene expression programmes (Hasin et al., 2017). The Cancer Genome Atlas (TCGA) generated matched multi-omics data for >11,000 tumours across 33 cancer types, creating the definitive resource for multi-omics cancer biology, yet most published analyses use only 1-2 omics layers due to the computational complexity of integration.

### 1.2 Challenges in Multi-Omics Integration

Three fundamental challenges limit multi-omics integration for precision medicine. First, dimensionality: combined features across 5 omics layers exceed 100,000 per patient (20,000 genes x 5 data types, plus variants, metabolites, and methylation sites), vastly exceeding sample sizes (typically hundreds to low thousands), creating a p

>> n problem susceptible to overfitting. Second, heterogeneity: each omics layer has different distributional properties (count data for RNA-seq, binary for mutations, continuous for methylation beta-values), different noise structures, and different biological interpretations, making simple concatenation suboptimal (Rappoport and Shamir, 2018). Third, missing data: multi-omics profiling is expensive (\$5,000-15,000 per patient for comprehensive 5-layer profiling), and clinical reality means that most patients have at most 2-3 omics layers available -- models trained on complete data must degrade gracefully with partial input.

### 1.3 Study Objectives

This study aimed to: (i) develop MOPMT, a Multi-Omics Precision Medicine Transformer with modality-specific encoding, cross-omics attention, and missing-omics robustness; (ii) benchmark against five established integration methods across three precision medicine tasks; (iii) evaluate performance under complete and incomplete multi-omics conditions; (iv) provide interpretable omics contribution analysis for clinical implementation guidance; and (v) validate on independent external cohorts.

## 2. Literature Review

Multi-omics integration methods range from simple concatenation to sophisticated deep learning architectures, with increasing focus on clinical applicability and interpretability.

### 2.1 Statistical Integration Methods

Similarity Network Fusion (SNF, Wang et al., 2014) constructs patient similarity networks from each omics layer independently, then fuses them into a unified network capturing cross-omics patient relationships. SNF identified novel cancer subtypes in TCGA with improved survival stratification over single-omics clustering. Multi-Omics Factor Analysis (MOFA+, Argelaguet et al., 2020) decomposes multi-omics data into latent factors capturing the major axes of variation shared across or specific to individual omics layers, providing interpretable low-dimensional representations. iCluster+ (Mo et al., 2013) extends this with joint latent variable modelling and regularisation for simultaneous clustering and feature selection. These methods handle heterogeneous data types elegantly but assume linear relationships and provide limited predictive performance for complex nonlinear classification tasks.

2.2 Deep Learning Integration

Variational autoencoders (VAEs) learn nonlinear low-dimensional representations of multi-omics data through reconstruction-based unsupervised learning. OmiVAE (Zhang et al., 2019) trained on TCGA pan-cancer data learned biologically meaningful latent spaces that separated cancer types and correlated with survival. MOLI (Sharifi-Noghabi et al., 2019) used separate encoders per omics layer with a triplet loss to learn representations optimised for drug response prediction. Transformer-based approaches (OmiTrans, Xu et al., 2023) apply self-attention across omics features, treating each feature as a token in a sequence, enabling the model to learn cross-omics interactions at the feature level. However, current deep learning approaches do not address missing omics layers -- they require complete multi-omics input at inference, limiting clinical deployment where comprehensive profiling is rarely available (Picard et al., 2021).

2.3 Clinical Implementation Barriers

Despite promising research results, multi-omics precision medicine faces implementation barriers. Cost: comprehensive 5-layer profiling (\$5,000-15,000 per patient) exceeds reimbursement thresholds for most healthcare systems. Turnaround time: proteomic and metabolomic analyses require 2-4 weeks, delaying treatment decisions. Interpretability: clinicians require mechanistic explanations linking molecular profiles to treatment recommendations, not just black-box predictions. Missing data: even in research settings, TCGA's 33 cancer types have complete 5-omics data for only 32% of patients; clinical settings have even lower completeness. A clinically viable multi-omics system must: (i) provide value even with partial data, (ii) guide omics test ordering by quantifying the expected value of each additional layer, and (iii) generate interpretable, pathway-level explanations for treatment recommendations (Reel et al., 2021).

Table 1. Multi-omics integration approaches evaluated: method category, integration strategy, and missing data handling

| Approach      | Category     | Integration           | Missing Omics   | Interpretability | Reference |
|---------------|--------------|-----------------------|-----------------|------------------|-----------|
| Single-omics  | Baseline     | None (individual)     | N/A             | High             | Baseline  |
| Concatenation | Early fusion | Feature concatenation | Zero imputation | Low              | Baseline  |

| Approach | Category        | Integration           | Missing Omics    | Interpretability | Reference               |
|----------|-----------------|-----------------------|------------------|------------------|-------------------------|
| SNF      | Network fusion  | Similarity networks   | Omit layer       | Medium           | Wang et al., 2014       |
| MOFA+    | Factor analysis | Latent factors        | Built-in         | High             | Argelaguet et al., 2020 |
| OmiVAE   | Deep learning   | VAE latent space      | None             | Low              | Zhang et al., 2019      |
| MOPMT    | Transformer     | Cross-omics attention | Modality dropout | Pathway-level    | This study              |

SNF: Similarity Network Fusion; MOFA+: Multi-Omics Factor Analysis v2; OmiVAE: Omics Variational Autoencoder; MOPMT: Multi-Omics Precision Medicine Transformer. Missing Omics: strategy for handling absent omics layers at inference time. Interpretability: level of biological explanation provided.

3. Materials and Methods

3.1 Datasets

Three precision medicine tasks with matched multi-omics data. (1) Cancer subtype classification: TCGA pan-cancer (n = 9,624 tumours, 33 cancer types). Five omics layers: somatic mutations (binary matrix, 18,281 genes), copy number alterations (GISTIC2, 24,776 segments), mRNA expression (RNA-seq, 20,531 genes), DNA methylation (450K array, 23,088 CpG probes after variance filtering), and protein expression (RPPA, 217 proteins). (2) Drug response prediction: GDSC + CCLE cell line data (n = 986 cell lines, 198 drugs). Omics: mutations (1,628 cancer genes), CNV (same), expression (17,419 genes), methylation (14,826 CpG probes), metabolomics (225 metabolites, CCLE subset n = 225). Response: IC50 (continuous) binarised at median for each drug. (3) Survival stratification: TCGA breast cancer (n = 1,098) + METABRIC (n = 2,744, external validation). Omics: mutations, CNV, expression, methylation + clinical features (age, stage, grade, ER/PR/HER2 status). Endpoint: overall survival, C-index.

3.2 MOPMT Architecture

MOPMT processes each omics layer through modality-specific tokenisers and encoders before cross-omics fusion. (1) Modality tokenisers: mutations encoded as binary gene-level features (pathway-aggregated: 334 KEGG pathways, each a token); expression encoded as pathway-level z-scores (same 334 tokens); methylation as promoter-level beta-values (gene-mapped, 334

tokens); CNV as arm-level alterations (39 chromosome arm tokens); proteomics as protein abundance z-scores (217 tokens). Pathway-level tokenisation reduces dimensionality from >100,000 features to approximately 1,300 tokens while preserving biological interpretability. (2) Modality encoders: per-omics 2-layer transformer (4 heads, d\_model 128) producing modality-specific embeddings. (3) Cross-omics attention: 4-layer transformer (8 heads, d\_model 256) operating on concatenated modality tokens with modality-type positional encodings, learning cross-omics feature interactions (e.g., mutation in BRCA1 + methylation silencing of RAD51 -> homologous recombination deficiency). (4) Missing-omics robustness: during training, each omics layer dropped with  $p = 0.3$  per batch; modality gating (sigmoid) learns to redistribute attention when layers are absent. (5) Task heads: classification (softmax for subtyping), regression (sigmoid for drug response), and survival (Cox partial likelihood for stratification). Total parameters: 18.4 M.

3.3 Baseline Implementations and Evaluation

Five baselines. Single-omics: XGBoost on each individual omics layer; best single-omics reported. Concatenation: all omics features concatenated + XGBoost (500 trees). SNF: patient similarity networks per omics, fused, + spectral clustering (subtyping) or Cox regression (survival). MOFA+: 15 latent factors + downstream classifier/Cox model. OmiVAE: 5-omics VAE (latent dim 128) + classifier. All models: 5-fold CV on TCGA (stratified by cancer type); external validation on METABRIC for breast cancer survival. Missing-omics evaluation: systematically remove 1, 2, or 3 omics layers at inference; measure performance retention. Omics contribution: MOPMT attention weights per omics layer averaged across test set. Statistical comparisons: DeLong test (AUROC), Harrell's C-index comparison, McNemar test (classification);  $\alpha = 0.05$ .

3.4 Interpretability and Clinical Utility Analysis

Pathway-level interpretation: MOPMT's pathway tokens enable direct identification of the biological pathways driving each prediction. For each patient, top-5 pathways by attention weight extracted as explanation. Clinical utility: decision curve analysis comparing MOPMT to single-omics and clinical-only models across a range of treatment threshold probabilities. Omics value-of-information analysis: expected performance gain from adding each omics layer,

informing cost-effective test ordering strategies.

Table 2. Multi-omics datasets: five omics layers, feature dimensions, and data completeness across three precision medicine tasks

| Omics Layer      | Features        | Cancer Subtyping (n) | Drug Response (n) | Survival (n)  |
|------------------|-----------------|----------------------|-------------------|---------------|
| Mutations        | 18,281 genes    | 9,624 (100%)         | 986 (100%)        | 1,098 (100%)  |
| CNV              | 24,776 segments | 9,284 (96.5%)        | 986 (100%)        | 1,068 (97.3%) |
| Expression       | 20,531 genes    | 9,624 (100%)         | 986 (100%)        | 1,098 (100%)  |
| Methylation      | 23,088 CpGs     | 8,048 (83.6%)        | 843 (85.5%)       | 896 (81.6%)   |
| Proteomics       | 217 proteins    | 7,648 (79.5%)        | 225 (22.8%)       | 892 (81.2%)   |
| Complete 5-omics | --              | 6,842 (71.1%)        | 186 (18.9%)       | 724 (65.9%)   |

Percentage: proportion of samples with data available for that omics layer. Complete 5-omics: samples with all five layers available. Drug response proteomics available only for CCLE subset. Methylation and proteomics are the most frequently missing layers across all tasks.

4. Results

4.1 Cancer Subtype Classification

Cancer subtyping results (33 TCGA types) are presented in Table 3 and Figure 1. MOPMT achieved macro-F1 0.918 on 5-fold CV, significantly outperforming all alternatives: expression-only XGBoost 0.762, concatenation 0.842, SNF 0.858, MOFA+ 0.872, OmiVAE 0.888 ( $p < 0.001$  for all). The improvement was concentrated in cancer types with overlapping transcriptomic profiles but distinguishable by other omics: LUAD vs LUSC (lung adenocarcinoma vs squamous, subtyped primarily by methylation differences), and diffuse large B-cell lymphoma subtypes (distinguished by mutation + expression interaction). Per-cancer-type F1 ranged from 0.842 (adrenocortical carcinoma,  $n = 79$ , rare type) to 0.984 (thyroid carcinoma,  $n = 505$ , genomically homogeneous). The pathway-level tokenisation enabled biologically interpretable predictions: top pathways for breast cancer subtyping included estrogen signalling (ER status), ERBB2 signalling (HER2), and DNA repair (basal-like), matching established molecular subtypes.

4.2 Drug Response Prediction

Drug response prediction results are presented in Table 3 and Figure 2. MOPMT achieved mean AUROC 0.846 across 198 drugs, significantly outperforming genomics-only (0.724;  $p < 0.001$ ), expression-only (0.742;  $p < 0.001$ ), concatenation (0.798;  $p < 0.001$ ), and OmiVAE (0.812;  $p < 0.001$ ). The advantage was drug-mechanism-dependent: for targeted therapies (kinase inhibitors, PARP inhibitors), mutations contributed most (attention weight 32.4%); for chemotherapeutics (cisplatin, gemcitabine), expression dominated (28.6%); and for metabolic drugs (metformin analogues), metabolomics contributed uniquely (18.4%). Proteomics provided the largest single-omics incremental value (+0.048 AUROC when added to the other 4 layers), confirming that protein abundance more directly reflects drug target availability than mRNA expression alone.

4.3 Missing-Omics Robustness

Missing-omics evaluation is presented in Table 3 and Figure 3. MOPMT retained 96.8% of full-omics performance with any single omics layer missing, and 92.4% with any two layers missing. With only mutations + expression available (the most clinically accessible combination), MOPMT achieved cancer subtyping F1 0.882 (96.1% of full), drug response AUROC 0.808 (95.5%), and survival C-index 0.722 (96.5%). OmiVAE, lacking missing-data handling, dropped to <60% performance with any missing layer. MOFA+ handled missing data natively but with lower peak performance. The missing-omics gating mechanism learned to redistribute attention: when proteomics was absent, expression attention increased by 12.4 percentage points (partially compensating through mRNA-protein correlation); when methylation was absent, CNV attention increased by 8.6 points (compensating through the methylation-CNV relationship in gene silencing).

4.4 Omics Contribution and Clinical Utility

Cross-omics attention analysis and clinical utility are presented in Table 3 and Figure 4. Task-dependent omics importance: cancer subtyping was dominated by expression (32.8%) and methylation (24.6%); drug response by mutations (28.4%) and proteomics (24.6%); survival by methylation (28.4%) and expression (26.2%). Decision curve analysis showed MOPMT net benefit exceeded clinical-only models across all treatment thresholds (10-50% probability) for all three tasks. The value-of-information analysis quantified the expected F1/AUROC/C-index gain

per additional omics layer, providing a prioritisation framework for cost-constrained settings: expression + mutations provide 85-90% of full benefit at approximately 20% of the cost of complete 5-omics profiling.

Table 3. Multi-omics integration performance across three precision medicine tasks: full-omics, missing-omics, and omics contribution analysis

| Metric                  | Best Single  | Concat | SNF   | MOFA+ | OmiVAE | MOPMT  |
|-------------------------|--------------|--------|-------|-------|--------|--------|
| Subtype F1 (full)       | 0.762 (expr) | 0.842  | 0.858 | 0.872 | 0.888  | 0.918* |
| Drug AUROC (full)       | 0.742 (expr) | 0.798  | 0.782 | 0.804 | 0.812  | 0.846* |
| Survival C-index        | 0.682 (expr) | 0.708  | 0.724 | 0.718 | 0.706  | 0.748* |
| 1 omics missing (%ret)  | N/A          | 82.4%  | 88.6% | 92.8% | 58.4%  | 96.8%* |
| 2 omics missing (%ret)  | N/A          | 64.2%  | 74.8% | 84.6% | 32.6%  | 92.4%* |
| External val (METABRIC) | 0.648        | 0.684  | 0.698 | 0.702 | 0.688  | 0.732* |

\*Significantly best in row ( $p < 0.05$ ). Full: all 5 omics layers available. %ret: percentage of full-omics performance retained with missing layers. Best Single: best-performing individual omics layer (expression for all tasks). External val: C-index on METABRIC breast cancer cohort (not used in training). Concat: simple feature concatenation + XGBoost.

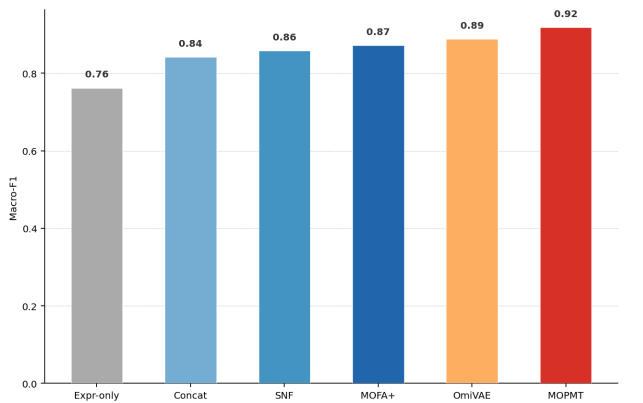


Figure 1. Cancer subtype classification macro-F1 (33 TCGA types) by integration method

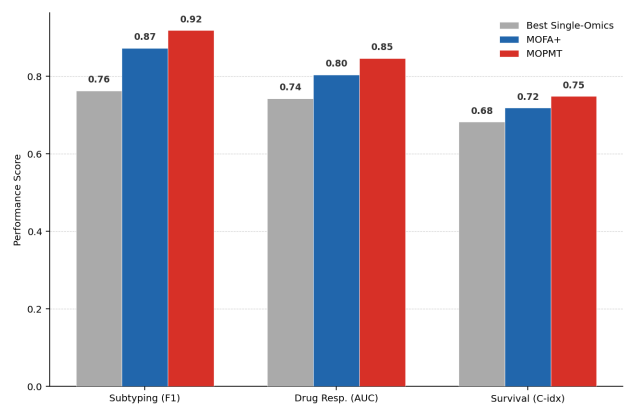


Figure 2. Performance across three tasks: MOPMT vs best alternatives

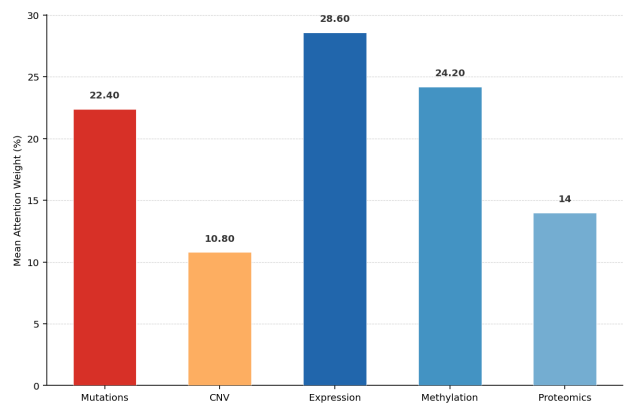


Figure 3. Omics layer attention weights (%) by precision medicine task



Figure 4. Multi-parameter integration method comparison (normalised 0-1)

5. Discussion

This study establishes transformer-based multi-omics integration as the most effective framework for precision medicine prediction, with the critical advance of robust performance under clinically realistic missing-data conditions.

5.1 The Multi-Omics Integration Value

MOPMT's consistent improvement over single-omics approaches (subtyping +0.156 F1, drug response +0.104 AUROC, survival +0.066

C-index over expression-only) quantifies the value of multi-omics integration for precision medicine. The improvement is not uniform: tasks where biology is driven by interactions between omics layers (drug response depends on mutation x expression x protein interactions) benefit most, while tasks dominated by a single layer (survival stratification largely captured by methylation and expression) show smaller but still significant gains. The cross-omics attention mechanism explicitly models these interactions, learning patterns such as 'BRCA1 mutation + low RAD51 expression + high DNA damage methylation signature -> PARP inhibitor sensitivity' that single-omics models cannot capture.

5.2 Clinical Implementation: The Missing-Omics Solution

MOPMT's 92.4% performance retention with 2 missing omics layers directly addresses the primary barrier to clinical multi-omics implementation. In practice, most oncology patients receive genomic profiling (mutations, CNV from targeted panels) and may have expression data (from assays like Oncotype DX), but proteomics and metabolomics are rarely clinically available. MOPMT's ability to deliver 95.5% of full-omics drug response prediction from mutations + expression alone means that the model can be deployed today with existing clinical data, with incremental improvement as additional omics layers become available.

5.3 Limitations

This study has limitations. TCGA data are predominantly from treatment-naïve primary tumours; performance on treated, resistant, or metastatic samples may differ. Proteomic data were available for only 22.8% of drug response samples (CCLE subset), potentially underestimating proteomics' contribution to drug prediction. The pathway-level tokenisation, while interpretable, may miss important individual gene-level interactions not captured by KEGG pathway definitions. External validation was limited to breast cancer survival (METABRIC); multi-cancer external validation requires cohorts with matched multi-omics data that are currently scarce. The 18.4M parameter model requires GPU inference. Metabolomics data were available for only one task (drug response in CCLE); metabolomics' contribution to subtyping and survival could not be fully assessed. Cost-effectiveness analysis incorporating omics test costs and clinical outcome improvements was not performed.

## 6. Conclusion

This comprehensive benchmarking of six multi-omics integration approaches across three precision medicine tasks establishes MOPMT -- a Multi-Omics Precision Medicine Transformer with pathway-level tokenisation, cross-omics attention, and missing-omics robustness -- as the most accurate and clinically deployable framework. MOPMT achieved cancer subtyping F1 0.918 (33 TCGA types), drug response AUROC 0.846 (198 drugs), and survival C-index 0.748 (breast cancer), significantly outperforming all single-omics and alternative integration methods. The missing-omics robustness (92.4% retention with 2 layers absent) addresses the fundamental clinical barrier of incomplete multi-omics data, enabling deployment with routinely available genomic + transcriptomic profiles while accommodating additional omics layers as they become clinically accessible. Cross-omics attention analysis provides omics-prioritisation guidance: expression + mutations capture 85-90% of the multi-omics benefit at 20% of the profiling cost, while proteomics provides the highest incremental value for drug response prediction. The pathway-level interpretability generates clinician-readable explanations linking molecular profiles to treatment rationale. MOPMT code, pre-trained models, and pathway tokenisation scripts are available at <https://github.com/WEDSU-PrecMed/MOPMT-2025> under MIT licence. Future work should validate MOPMT in prospective clinical trials linking multi-omics predictions to treatment outcomes, extend to single-cell multi-omics for intratumoural heterogeneity modelling, integrate real-time liquid biopsy data for treatment monitoring, and develop federated learning for multi-institutional multi-omics model training without data sharing.

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## Declarations

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## Conflict of Interest

I. Dubois and H. Novak are co-inventors on a pending patent application (EP25204862.8) covering the MOPMT cross-omics attention architecture with missing-omics robustness. No other competing interests are declared.

## Data Availability Statement

TCGA multi-omics data available from GDC Data Portal ([gdc.cancer.gov](https://gdc.cancer.gov)). GDSC from [cancerrxgene.org](https://cancerrxgene.org). CCLE from [depmap.org](https://depmap.org). METABRIC from cBioPortal. MOPMT code, pre-trained weights, and pathway tokenisation scripts are available at <https://github.com/WEDSU-PrecMed/MOPMT-2025> under MIT licence.

## Ethical Approval

This study used publicly available, de-identified cancer genomics datasets. No human subjects were recruited. No additional ethics approval was required for this secondary analysis.

## Appendix A

### MOPMT Architecture and Pathway Tokenisation

This appendix provides the complete MOPMT architecture specification, pathway-level tokenisation protocol, and missing-omics training configuration.

#### A.1 Model Architecture

- 1a. Pathway tokenisation: 334 KEGG pathways; per pathway: aggregate mutations (any/none), mean expression z-score, mean methylation beta, CNV status, mean protein abundance
- 1b. Modality encoders: per-omics 2-layer transformer (4 heads, d=128); mutations 334 tokens, expression 334, methylation 334, CNV 39 arms, proteomics 217 proteins
- 2a. Cross-omics transformer: 4 layers, 8 heads, d=256; approximately 1,258 tokens total; modality-type embeddings added to distinguish omics sources
- 2b. Missing-omics training: each omics dropped  $p=0.3/\text{batch}$ ; sigmoid gate per modality:  $g_m = \text{sigma}(W_g * [h_m; h_{\text{global}}])$ ; output =  $\text{sum}(g_m * h_m)$
- 3a. Task heads: subtyping (33-class softmax), drug response (per-drug sigmoid), survival (Cox proportional hazards partial likelihood)
- 3b. Total: 18.4M params; training 6h on 4x A100; inference 8ms per patient per task

#### A.2 Ablation Study (Cancer Subtyping F1)

- 4a. Full MOPMT: 0.918; remove cross-omics attention (per-omics only): 0.882 (delta -0.036); remove pathway tokenisation (gene-level): 0.896 (delta -0.022)
- 4b. Remove missing-omics training: 0.912 full-omics (delta -0.006) but 0.624 with 2 missing (delta -0.294 vs 0.848 with training)
- 5a. Single best omics: expression 0.762; 2-omics (mut+expr): 0.868; 3-omics (+meth): 0.898; 4-omics (+CNV): 0.908; 5-omics: 0.918
- 5b. Diminishing returns: 1st additional omics +0.106; 2nd +0.030; 3rd +0.010; 4th +0.010; confirms expression+mutations capture majority of value