Pathogen-X: A Cross-modal Genomic Feature Trans-align Network for Enhanced Survival Prediction from Histopathology Images

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INTRODUCTION

- Genomic data is a powerful predictor for survival than pathology data but it is costly and inaccessible
- Cross Modal genomic feature translation and alignment network uses histopathology image for enhanced survival prediction
- It enhances the weaker imaging signals with stronger genomic signals

PATHOGEN-X

Modality

- Training – histopathology and genomic data
- Testing – histopathology data

Cross Modality translator

- Translates image features to genomic compatible latent space(P(I)) and back to image compatible latent space
- Transformer-based pathology encoder and genomic decoder

EXPERIMENTS

- Compared with Mean-MIL, Max-MIL, Attn-MIL, Trans-MIL, SimL, genomic survival models
- Survival analysis of high vs. low-risk groups
- Effect of latent and translation loss analyzed

METHODOLOGY

Genomic feature projection Network

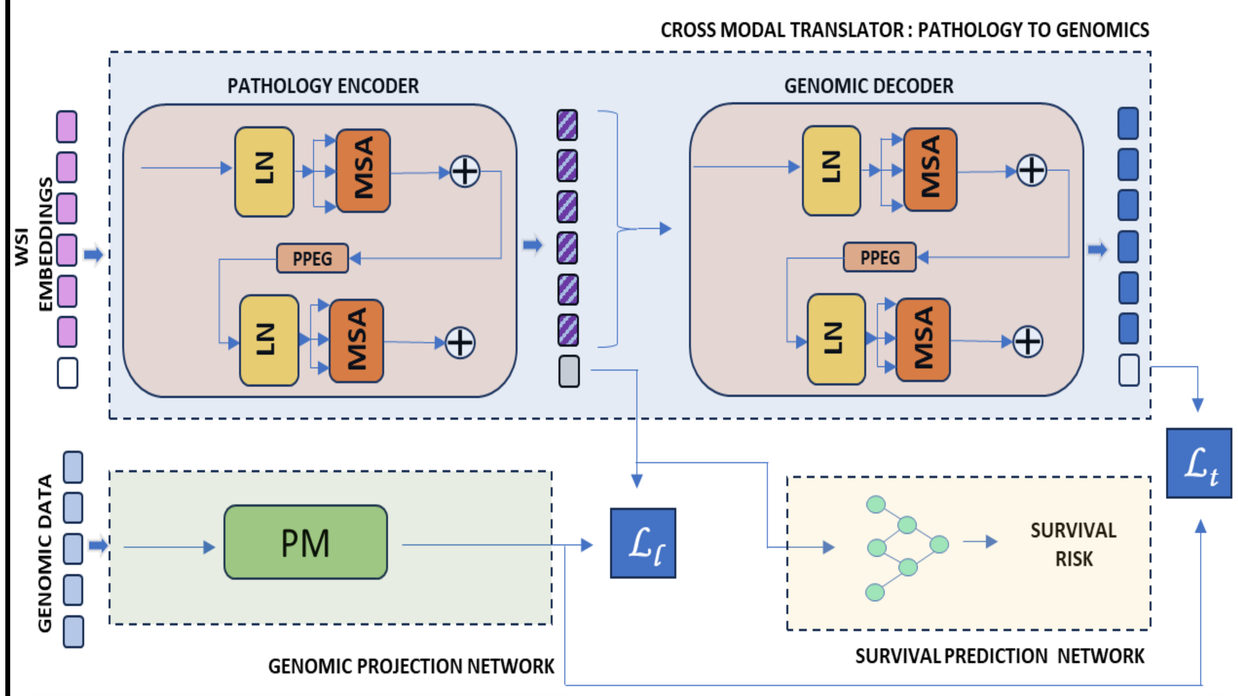
- Maps genomic data to latent representation G(I) aligned with pathology latent embeddings P(I)

Survival prediction Network

- Uses a multi-layer perceptron on P(I) to predict cancer survival risk
- Cox Loss – Optimizes survival prediction

Cross Modal Alignment and Translation

- Latent Loss (L(I)) - Aligns pathology and genomic latent embeddings
- Translation Loss (L(t)) - Aligns genomic encoder and decoder embeddings



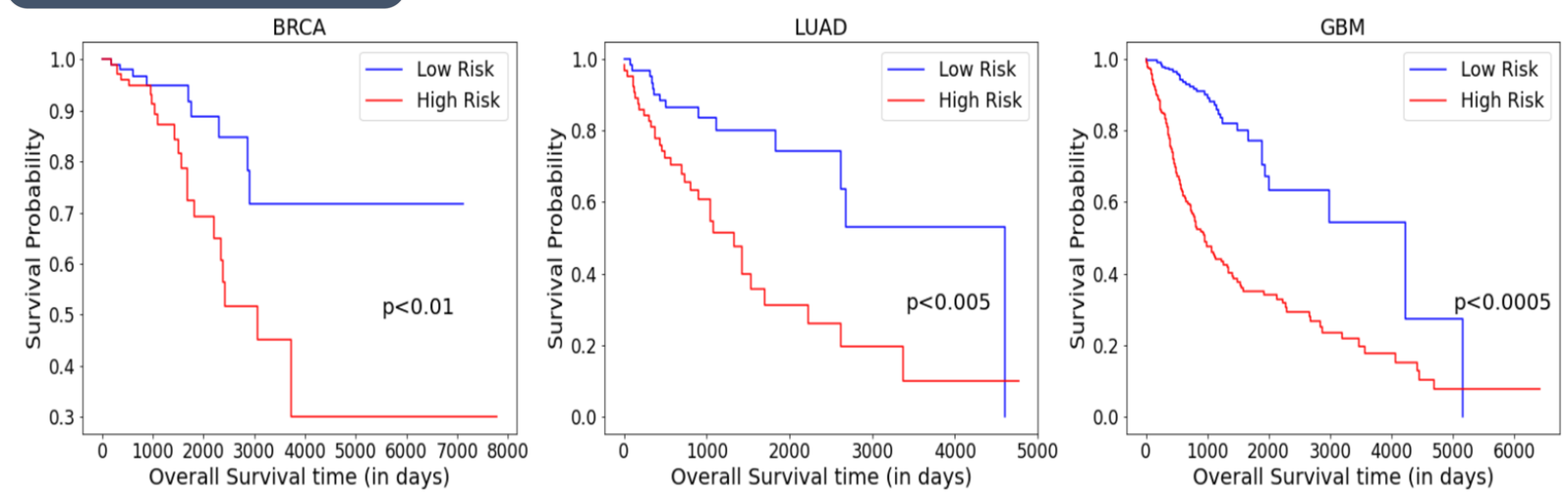
The cross-modal genomic feature trans-align network (PathoGen-X) features four main components: a pathology encoder, a genomic decoder, a genomic projection matrix (PM) and a survival prediction module.

RESULTS

- **Genomic predictive power :** Higher predictive power than pathology
- **Performance :** Outperforms the second-best method on BRCA, GBM and LUAD
- **Feature correlation :** Improved genomic-image correlation post alignment
- **Risk stratification :** High vs low risk group show significant survival gap ($p<0.01$)
- **Loss contribution :** The latent and translation loss together led to more improvement

Train	Test	Methods	BRCA	LUAD	GBM	Mean
G	G	Neural-Cox	0.67 ± 0.088	0.63 ± 0.019	0.86 ± 0.036	0.72
I	I	MaxMIL	0.57 ± 0.042	0.52 ± 0.021	0.66 ± 0.016	0.58
I	I	MeanMIL	0.61 ± 0.086	0.58 ± 0.032	0.73 ± 0.037	0.64
I	I	A-MIL	0.61 ± 0.083	0.59 ± 0.054	0.74 ± 0.042	0.64
I	I	TransMIL	0.59 ± 0.058	0.58 ± 0.006	0.79 ± 0.034	0.65
I+G	I	SimL	0.61 ± 0.085	0.60 ± 0.015	0.74 ± 0.014	0.65
I+G	I	PathoGen-X	$\mathbf{0.67 \pm 0.020}$	$\mathbf{0.62 \pm 0.008}$	$\mathbf{0.81 \pm 0.0023}$	**0.70**

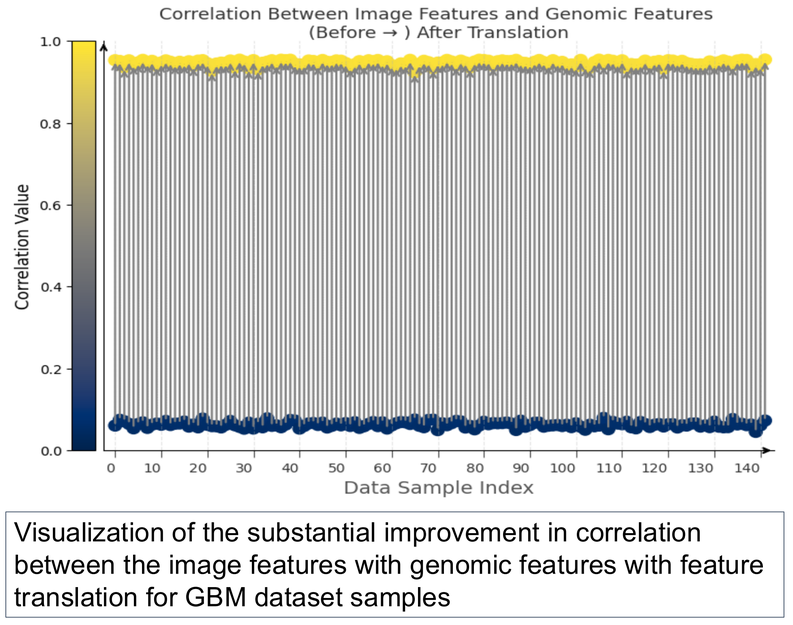
Survival prediction results (cross-validated on four-folds) on TCGA-BRCA, TCGA-LUAD, and TCGA-GBM datasets evaluated using C-index. The "Train" and "Test" columns indicate the modality used for training and testing, where "I" represents pathology images and "G" denotes genomic data. The best test results achieved using only imaging data are shown in **bold**.



The Kaplan-Meier curves of our model on the three datasets. We used median risk to stratify patients into low and high-risk groups.

Alignment Loss	BRCA
L_l	0.64
L_t	0.65
$L_l + L_t$	0.67

Ablation study analyzing the impact of different alignment loss variations on the TCGA-BRCA dataset



Visualization of the substantial improvement in correlation between the image features with genomic features with feature translation for GBM dataset samples

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