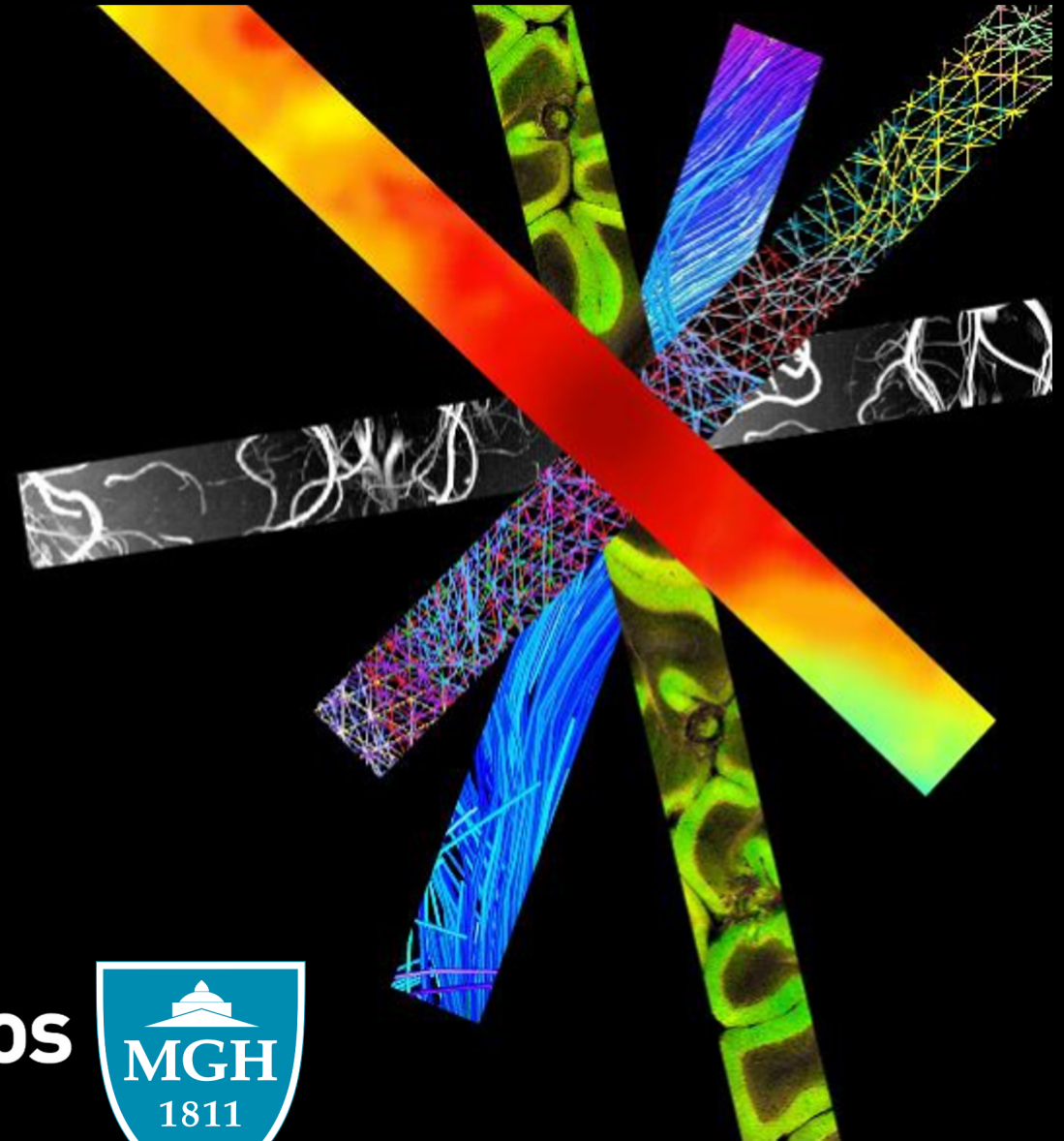# Deep Learning-based Prediction of Breast Cancer Tumor and Immune Phenotypes from Histopathology

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Tiago Gonçalves, Dagoberto Pulido-Arias, Julian Willett, Katharina V. Hoebel, Mason C. Cleveland, Syed Rakin Ahmed, Elizabeth Gerstner, Jayashree Kalpathy-Cramer, Jaime S. Cardoso, Christopher P. Bridge*, Albert E. Kim*
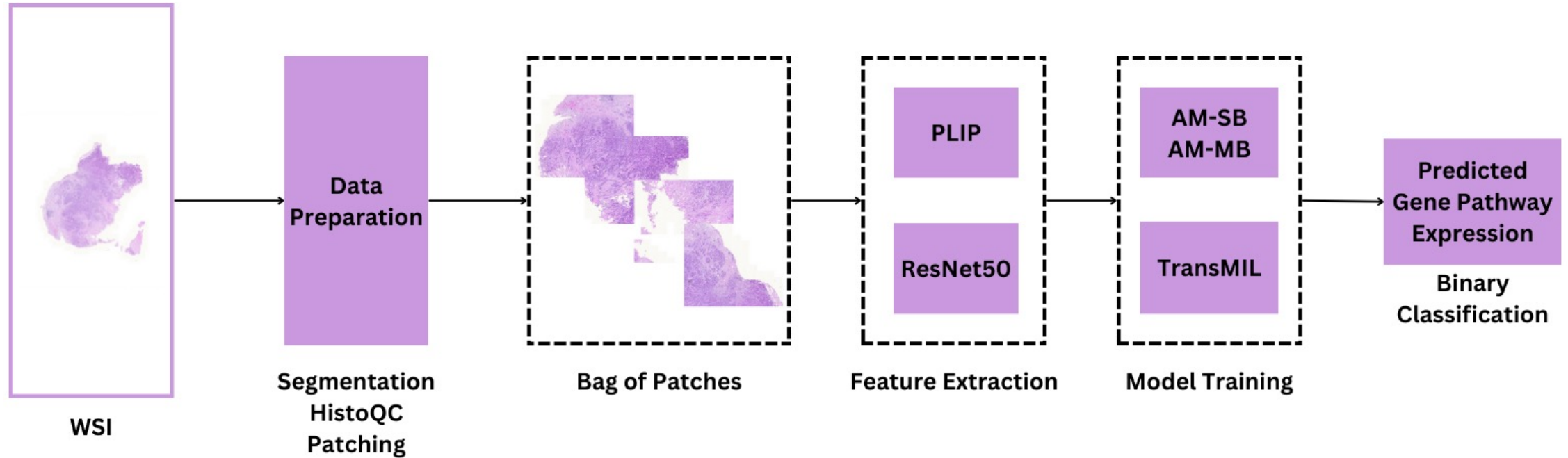
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Tumor and immune phenotypes from histopathology: context and motivation

- Tumor and immune phenotypes are **strongly linked with therapeutic efficacy and risk of metastasis** in breast cancer

- However, to date, **there is not a widely available method** to reliably characterize these facets of the tumor microenvironment (TME)

- Given this unmet clinical need, we applied multiple instance learning (MIL) algorithms to **assess activity of clinically relevant gene expression pathways from the hematoxylin and eosin (H&E) slide** of primary breast tumors

Our proposed pipeline

WSI → Data Preparation (Segmentation, HistoQC, Patching) → Bag of Patches → Feature Extraction (PLIP, ResNet50) → Model Training (AM-SB, AM-MB, TransMIL) → Predicted Gene Pathway Expression (Binary Classification)

Model architecture is not important for the performance, but the feature extraction strategy is

Task	Architecture & Features		
	AM-SB ResNet50 / PLIP	AM-MB ResNet50 / PLIP	TransMIL ResNet50 / PLIP
B-cell proliferation	0.6974 / **0.7755**	**0.7322** / 0.7735	0.6960 / 0.7673
T-cell mediated cytotoxicity	0.7149 / 0.7703	**0.7564** / **0.7770**	0.7223 / 0.7196
Angiogenesis	0.7042 / **0.7435**	**0.7053** / 0.7213	0.7019 / 0.7214
Epithelial-mesenchymal transition	**0.8110** / 0.7848	0.8023 / **0.8082**	0.7545 / 0.7934
Fatty acid metabolism	**0.6323** / **0.6030**	0.6294 / 0.5920	0.5258 / 0.5634
Glycolysis	**0.7996** / 0.8118	0.7954 / **0.8330**	0.7834 / 0.8045
Oxidative phosphorylation	0.6894 / 0.7145	**0.6926** / **0.7332**	0.6699 / 0.6826
Immunosuppression	0.7996 / 0.8458	**0.8133** / **0.8542**	0.7572 / 0.8113
Antigen processing and presentation	0.7450 / 0.7806	**0.7599** / **0.7924**	0.7503 / 0.7342
Cell cycle	0.7768 / **0.7939**	**0.7809** / 0.7852	0.7121 / 0.7229

1. While the AM-SB and AM-MB model architectures outperform TransMIL prediction of all gene expression tasks, the increase in performance was marginal
2. Models trained with PLIP-derived features generally perform better

Do we have any insight about what the model might be learning?
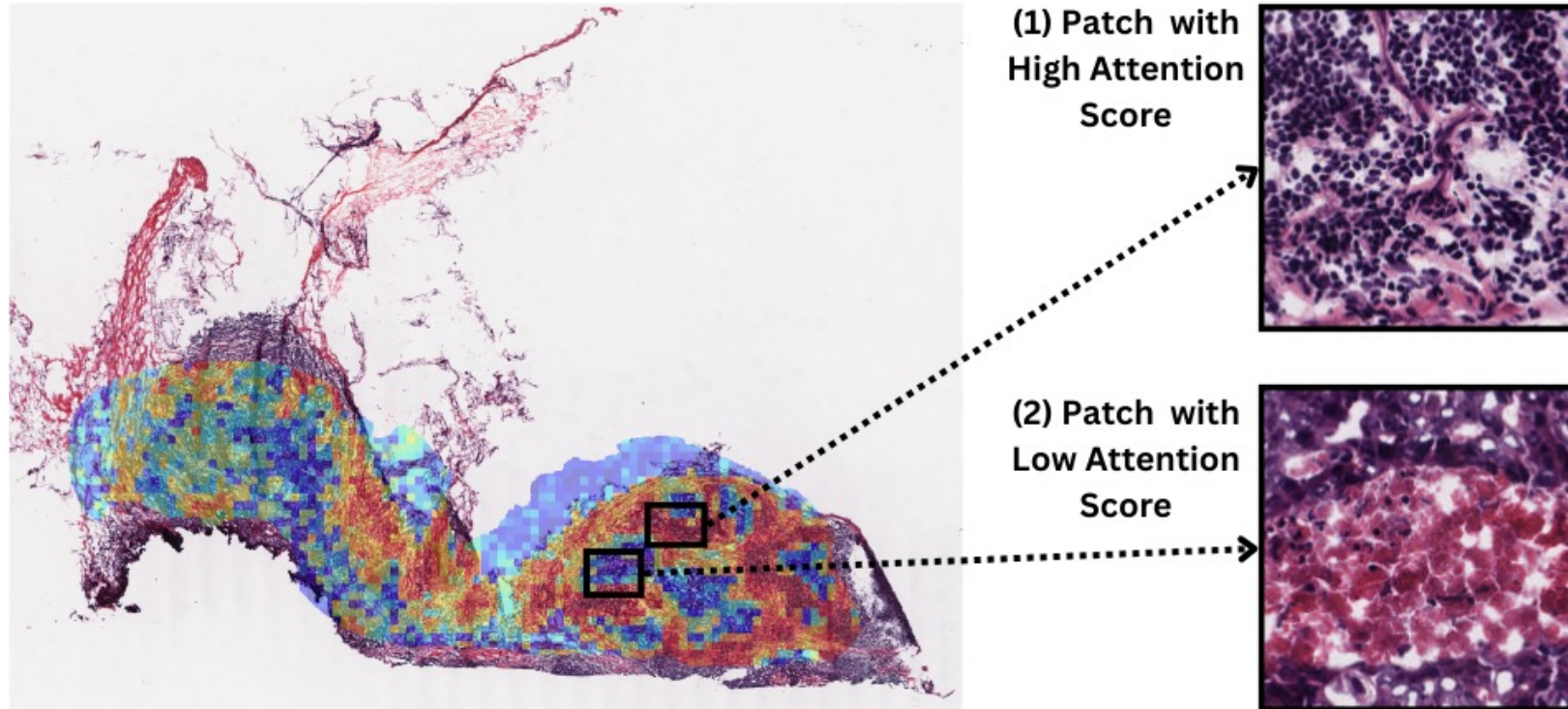
Attention map obtained using the AM-SB architecture for a WSI predicted to have a high-degree of T-cell mediated cytotoxicity

(1) Illustrates abundant tumor-infiltrating lymphocytes without tumor cells, which are suggestive of high immune activity
(2) Demonstrated areas of tumor necrosis and minimal lymphocytes, consistent with low immune activity

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