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# Expression-Based Molecular Subtyping & Classification of Bladder Cancer TCGA Data

Artificial Intelligence in Medicine (AIM) Lab

# A Consensus Molecular Classification of Muscle-Invasive Bladder Cancer (MIBC)

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European Association of Urology (EAU).

# Overview

**Bladder Cancer:**

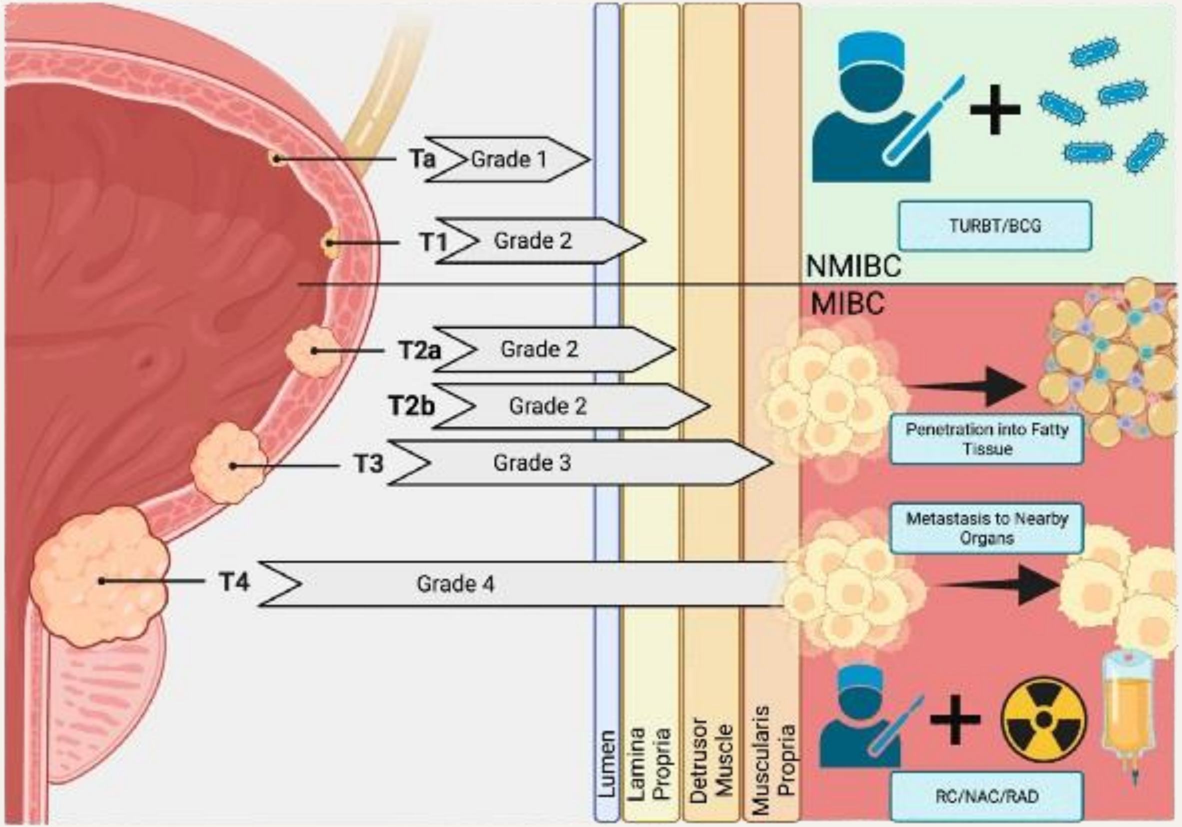
Urothelial Carcinoma Originating in Tissues of the Urinary System

**Non-Muscle Invasive Bladder Cancer**

Superficial Cancer Confined to Mucosa Layer

**Muscle-Invasive Bladder Cancer**

Aggressive Cancer Penetrating Muscle Layer




https://www.mdpi.com/2227-9059/11/2/539

# Introduction

**Existing Classification Systems:**

Diversity of Molecular Subtypes Impedes Clinical Application

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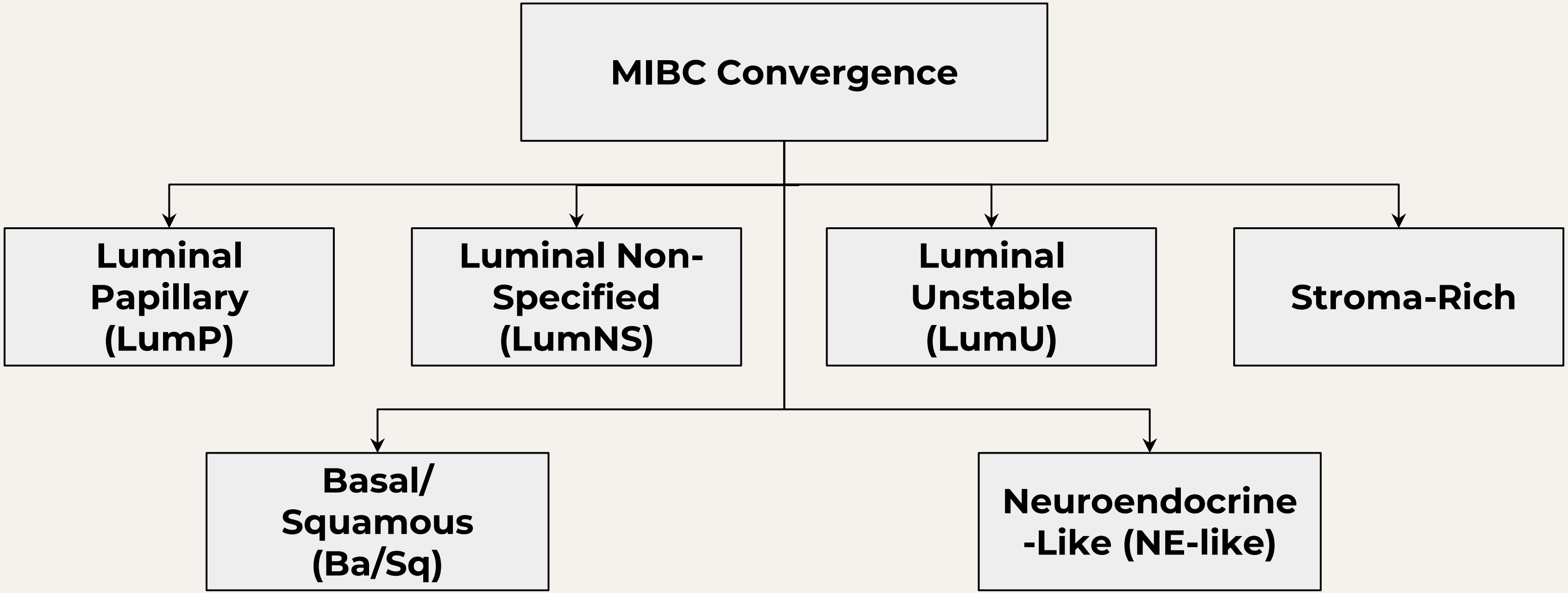
Lack of Naming Convention + Data Variability

**Research Objective:**

"Achieve International Consensus of MIBC Molecular Subtypes that Reconciles Published Classification Schemes"

# Consensus Classification

**Implementation:** Nearest-Centroid Transcriptomic Classifier in R



# Analytical Workflow

**Patch Extraction**

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**Feature Extraction**

⇓

**Multiple Instance Learning (MIL)**

⇓

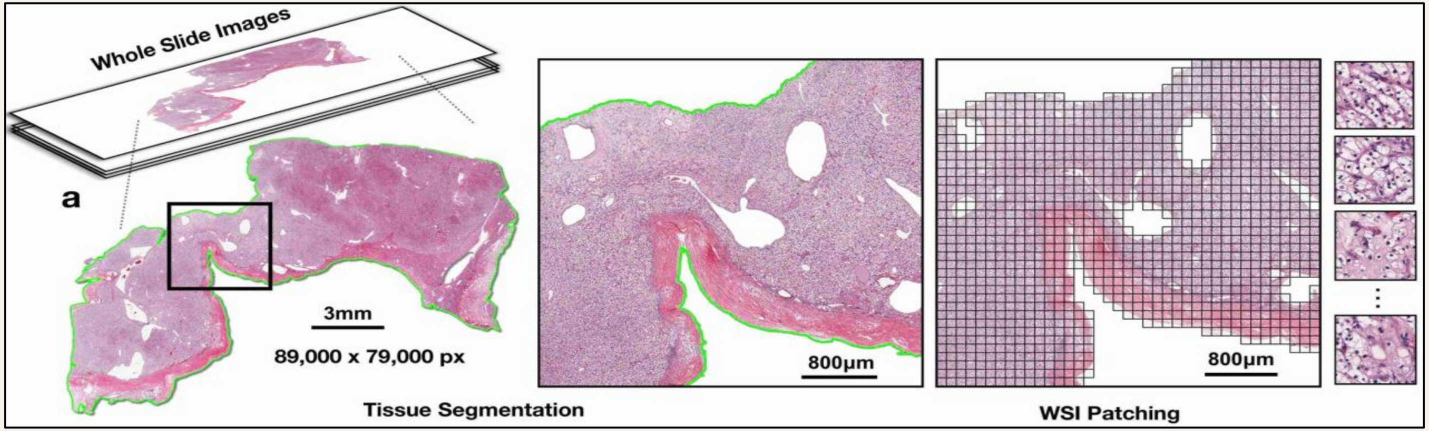
**Information Visualization**

# Patch Extraction

**Purpose:** Facilitate Localized Deep Learning

**Input:** Masks Pre-Selected from HistoQC

**Output:** 1,500 Patches Per Whole Slide Image



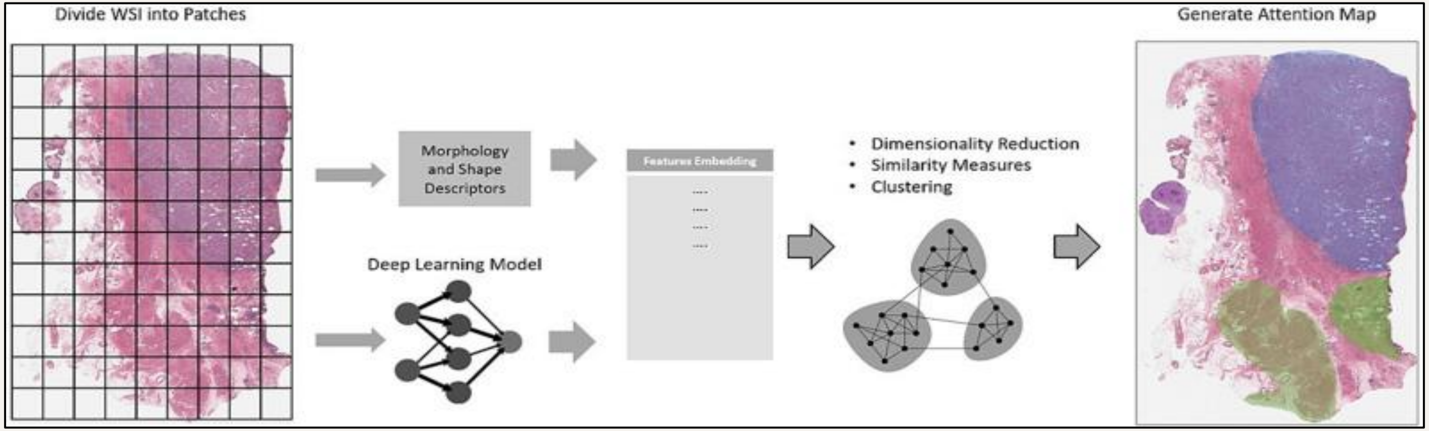

https://pixelscientia.com/articles/from-patches-to-slides/

# Feature Extraction

**Purpose:** Meaningfully Represent Tissue Characteristics

**Input:** 1,500 Patches Per Whole Slide Image

**Output:** 458 Diagnostic + 463 Frozen .h5 Files




https://www.sciencedirect.com/science/article/pii/S215335392300149

# Feature Encoders

| CTransPath | Lunit Dino |
| --- | --- |
| Pre-Trained Vision Transformer for Unsupervised Contrastive Learning | Pre-Trained Vision Transformer for Self-Supervised Learning |
| **Phikon** | **PLIP** |
| Pre-Trained Vision Transformer for Self-Supervised Learning | Pre-Trained Vision Transformer for Pathology Image Retrieval |
| **UNI** | **vit** |
| Pre-Trained Vision Transformer for Self-Supervised Learning | Pre-Trained Vision Transformer for Self-Supervised Learning |

# Multiple Instance Learning

**Purpose:** Analyse Extracted Features at Bag-Level

**Input:** 458 Diagnostic + 463 Frozen .h5 Files for 20x Mag

**Output:** 90 Checkpoint + Output .pt Files per Model

**Models:**

1. DeepMIL
2. TransMIL
3. ClamSB

**Data Folds:**

1. Fold #1
2. Fold #2
3. Fold #3

**Relevant Metrics:**

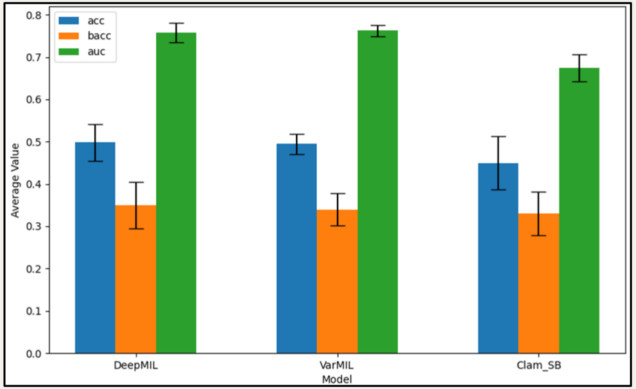
1. Accuracy
2. Bal. Accuracy
3. AUC

**Others:**

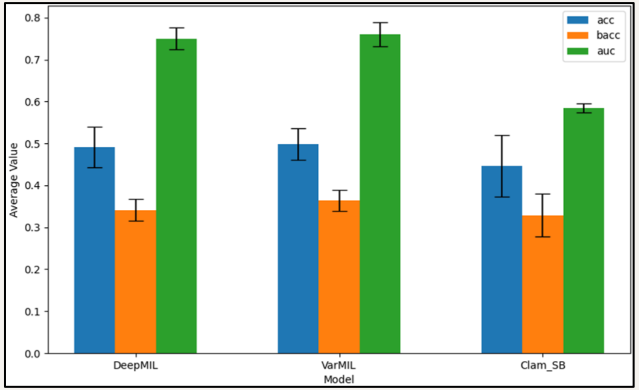
1. Time
2. Recall
3. Precision
4. F1-Score

# DIAGNOSTIC

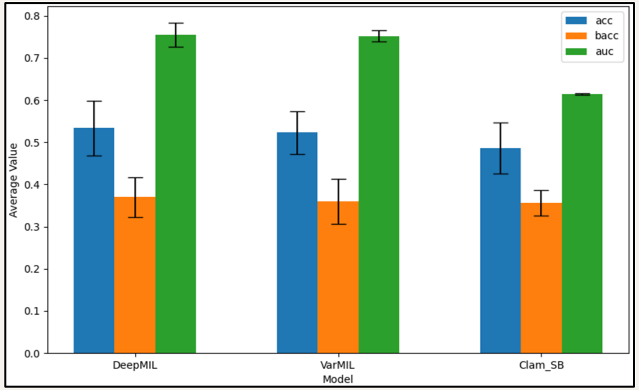
## CTransPath



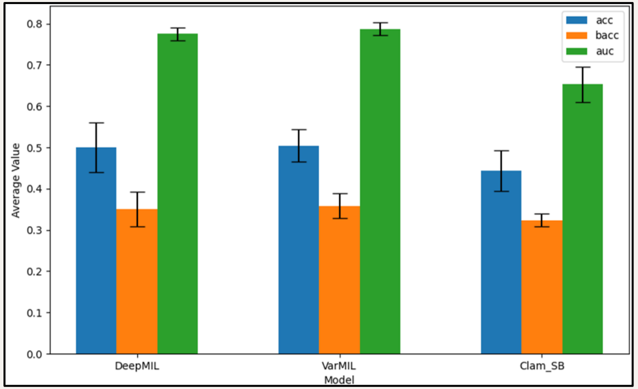

## Phikon



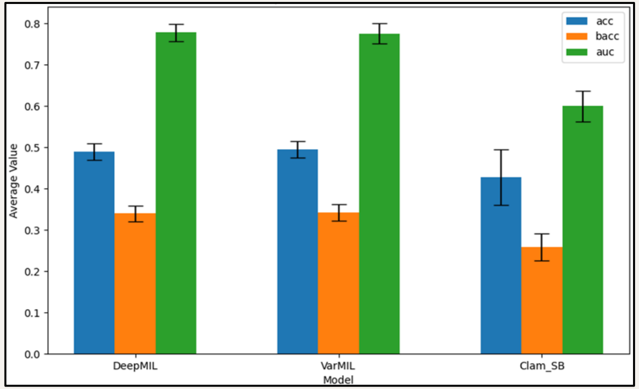

## UNI



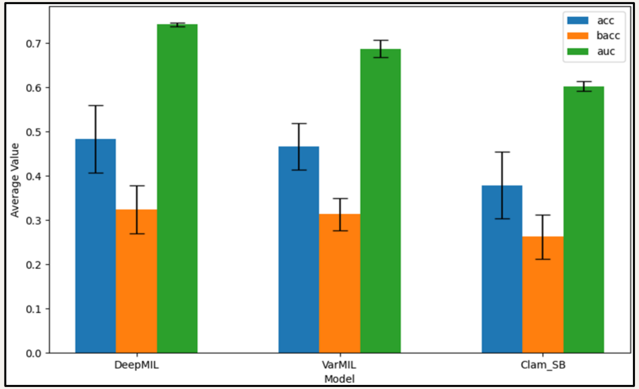

## Lunit-Dino




## PLIP

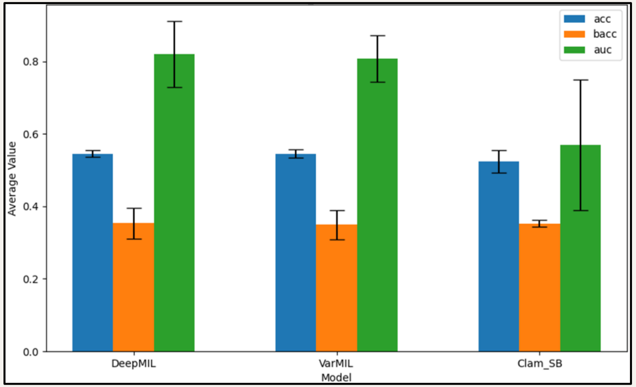



## vit



# FROZEN

## CTransPat

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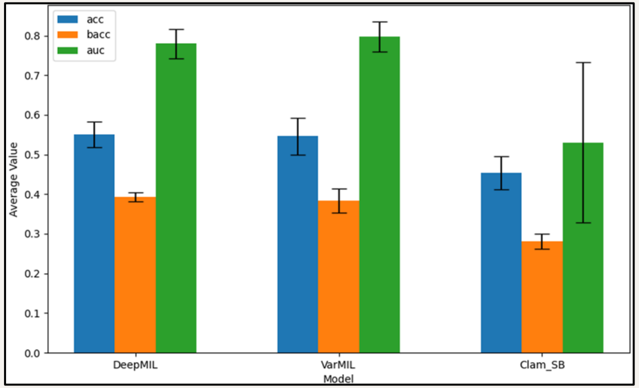


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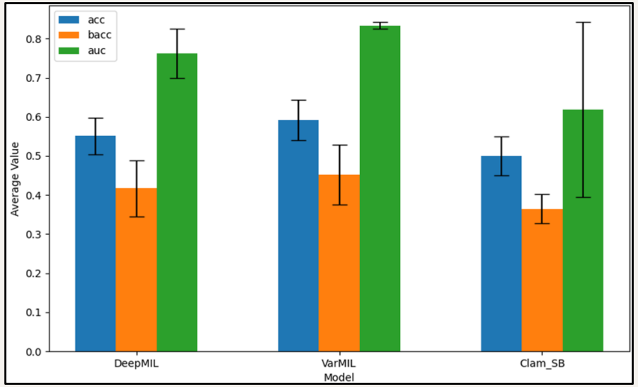


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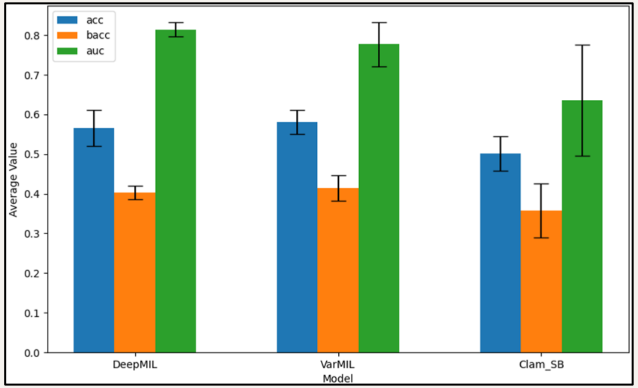
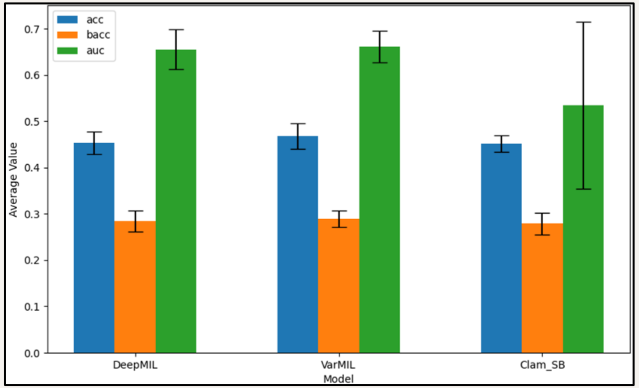
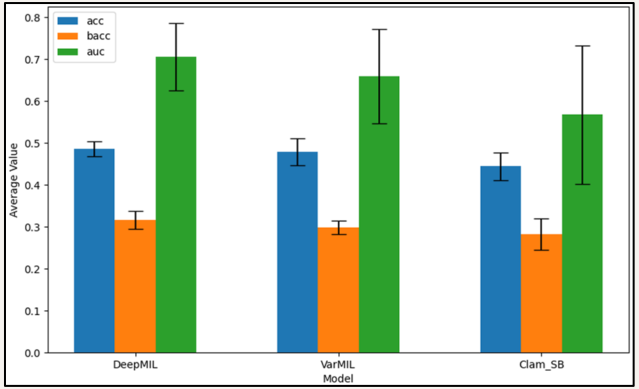



## PLIP




## vit



# Summary of Findings

**Observations:**

- CTransPath, Phikon and UNI were the Highest Performing Encoders
- DeepMIL and VarMIL Consistently Provided the Highest Metrics
- AUC Varied the Most Between Models while BACC Varied the Least

**Future Work:**

- Implement Hyperparameter Tuning (Learning Rate, Weight Decay etc.)
- Experiment with Multi-Headed Attention Mechanisms or Hybrid Variants
- Use Cross-Validation to Prevent Over-Fitting and Increase Robustness

# Information Visualization

**Purpose:** Determine Relationships Between Subtypes

**Input:** 458 Diagnostic + 463 Frozen .h5 Files for 20x Mag., Manifest File (patient_id, slide_id, subtype, slide_path)

**Output:** UMAP Plots

## Slide-Level

Mean Pooling of 1,500 Patches + Filtering of Features with No Subtypes

Eg: (1,500, 768) → (1, 768)

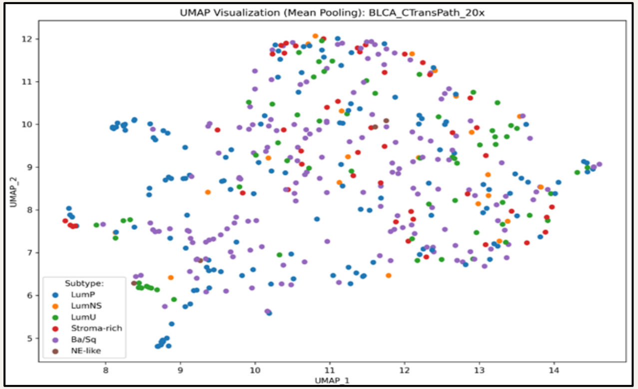
## Patch-Level

Random Selection of 150 Patches + Filtering of Features with No Subtypes

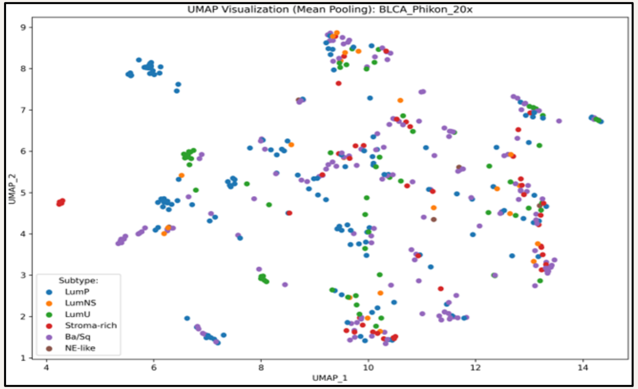
Eg: (1,500, 768) → (150, 768)

# DIAGNOSTIC (Slide-Level)

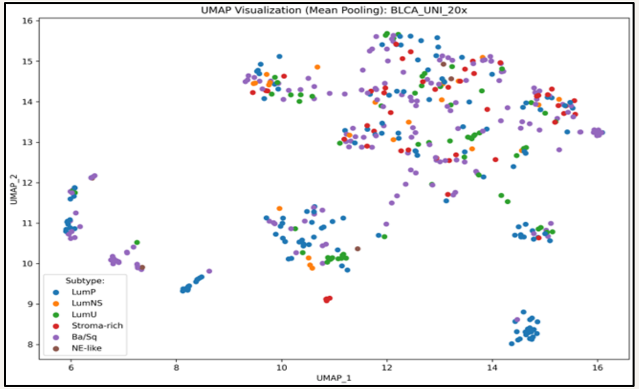
## CTransPath



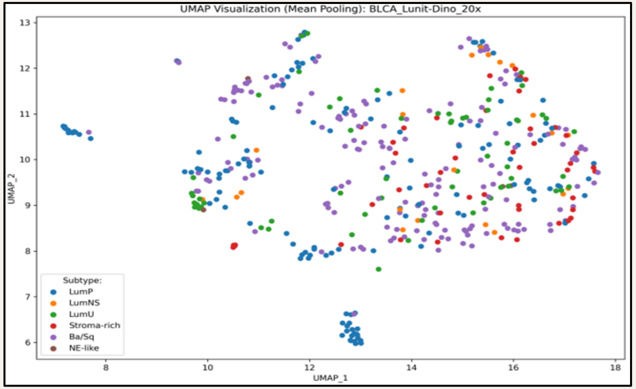

## Phikon



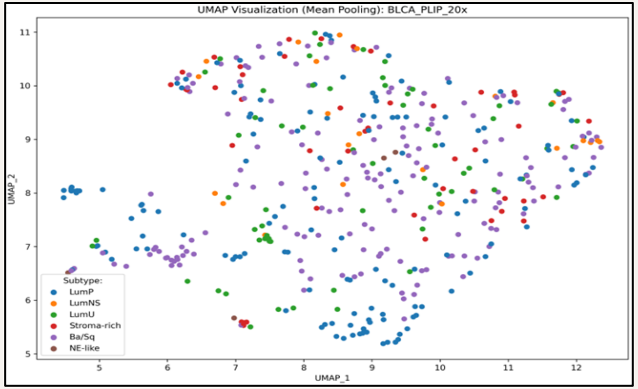

## UNI



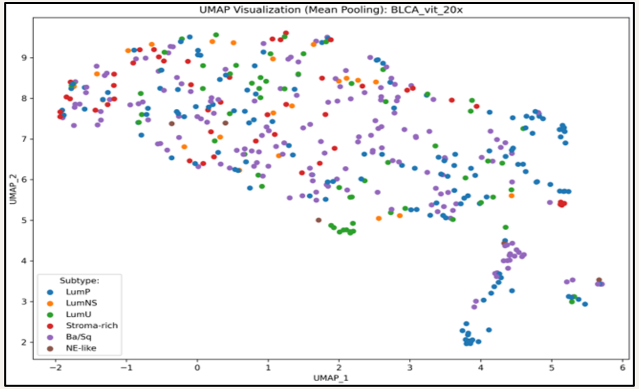

## Lunit-Dino




## PLIP

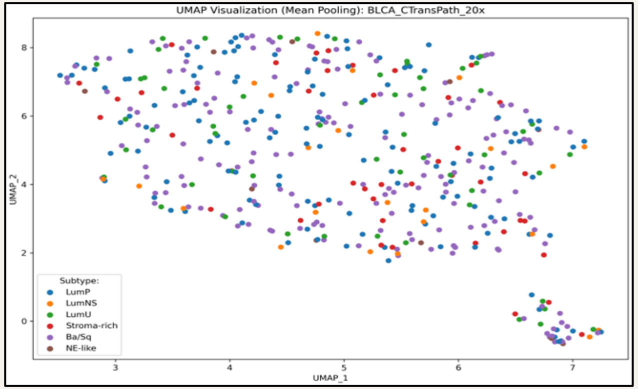



## vit

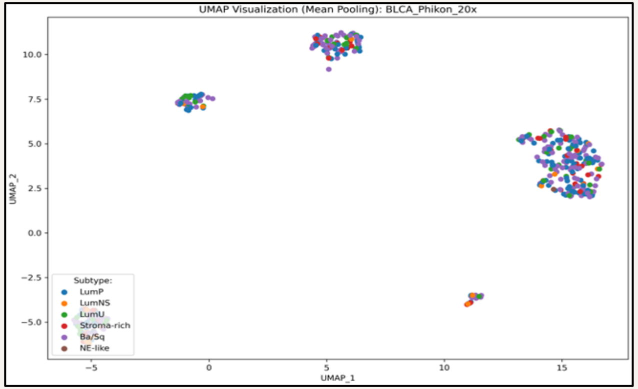


# Frozen (Slide-Level)

## CTransPath




## Phikon

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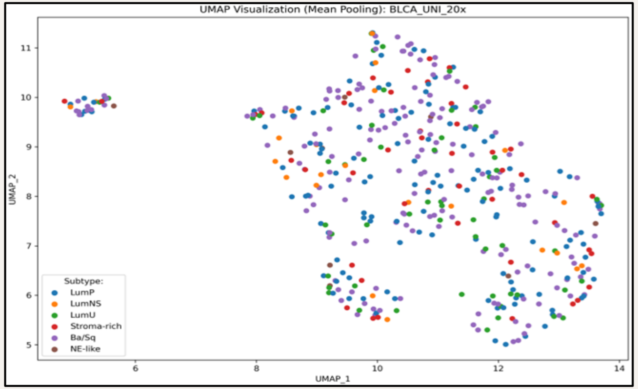
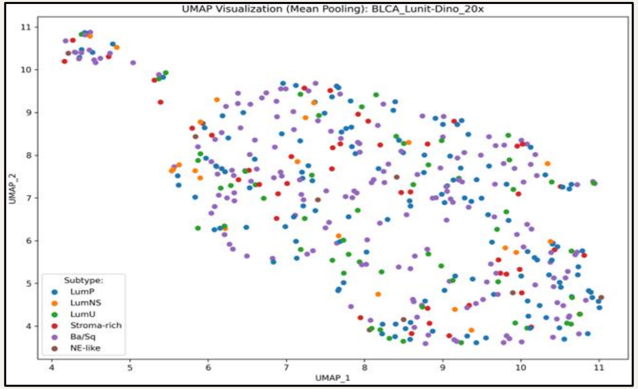



## Lunit-Dino

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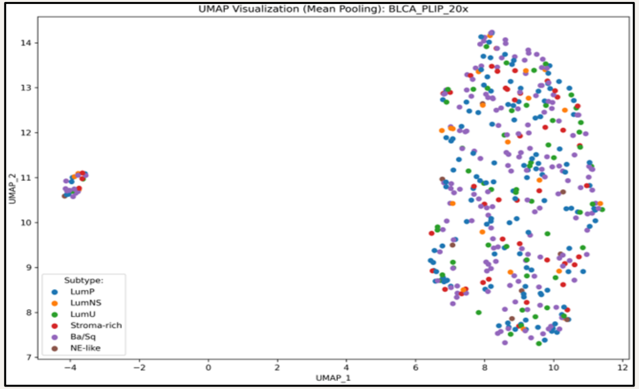
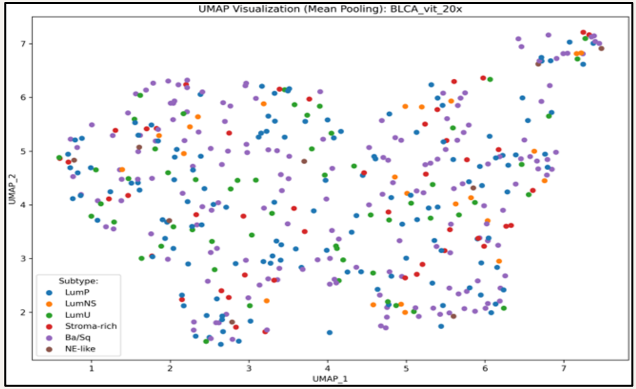
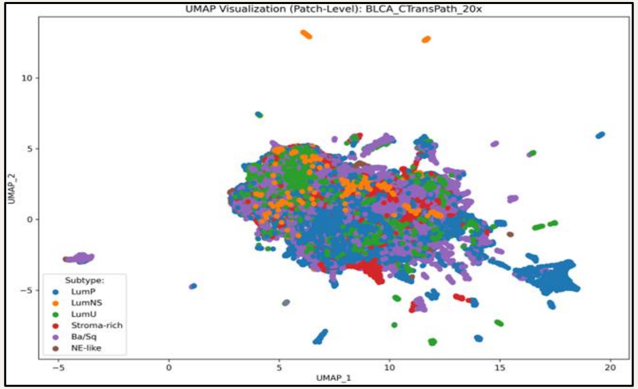



## vit

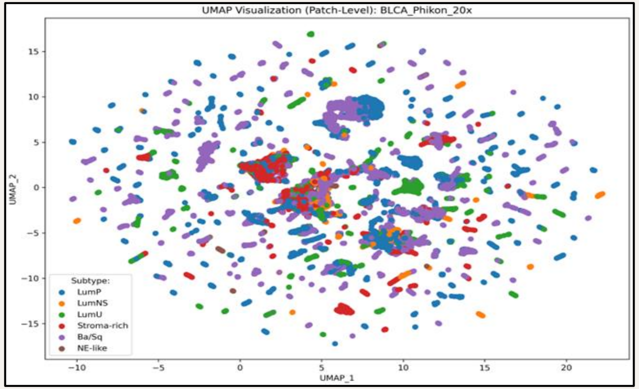


# DIAGNOSTIC (Patch-Level)

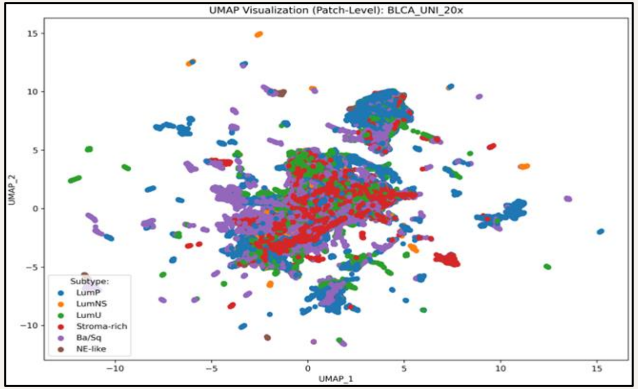
## CTransPath



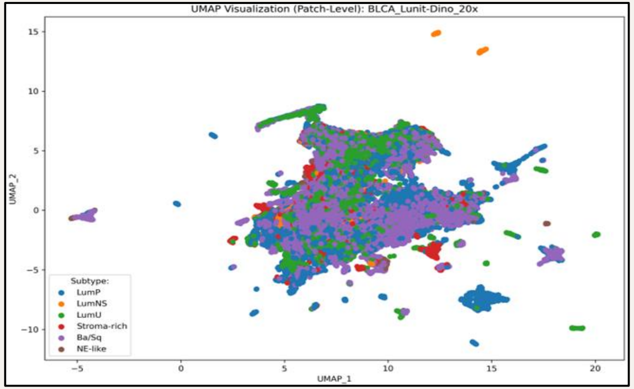

## Phikon




## UNI




## Lunit-Dino

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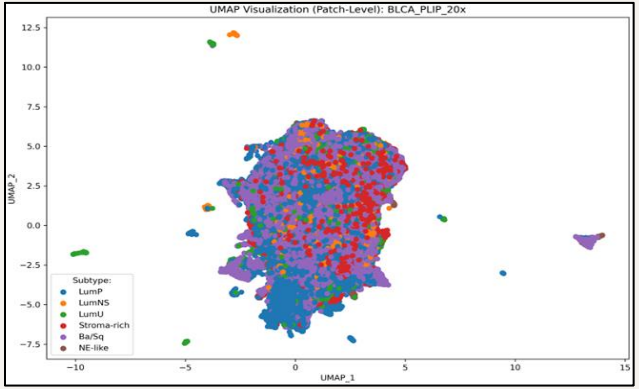
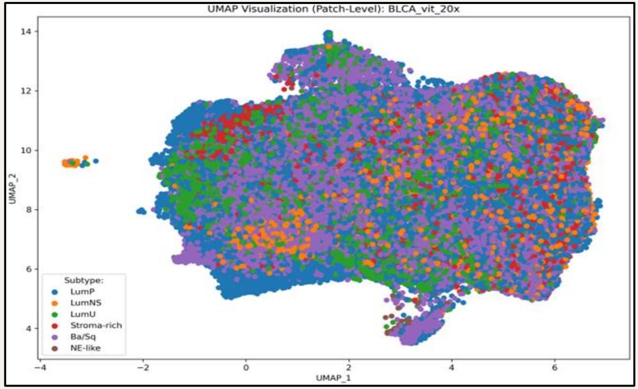
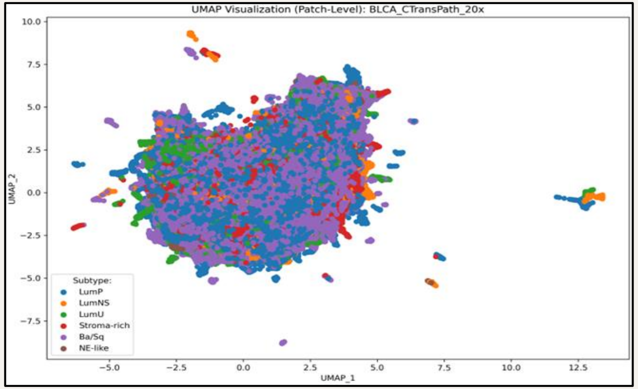



## vit

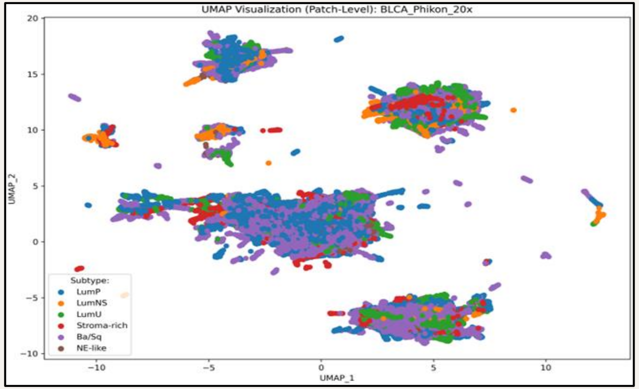


# FROZEN (Patch-Level)

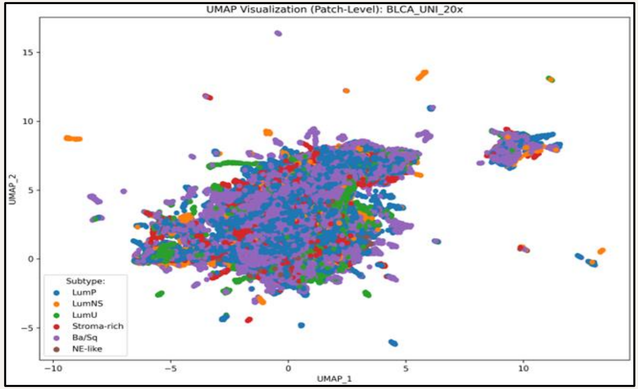
## CTransPath



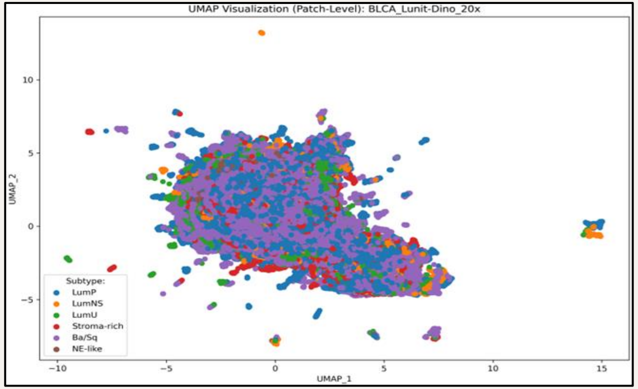

## Phikon




## UNI




## Lunit-Dino

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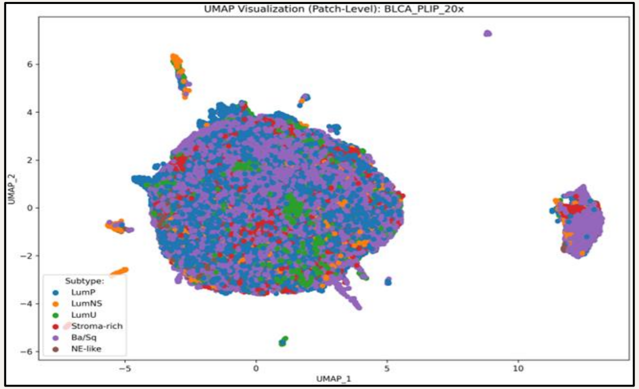
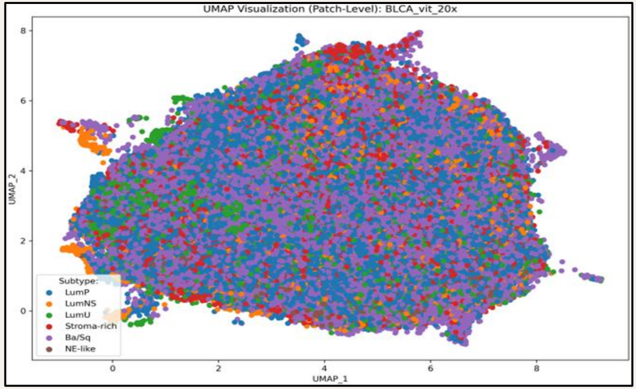



## vit



# Summary of Findings

**Observations:**

- Patch-Level UMAPs Provided Higher Granularity than Slide-Level UMAPs
- Patch-Level UMAPs Capture Data Diversity Better than Slide-Level UMAPs
- Patch-Level UMAPs Retain Local Patterns Better than Slide-Level UMAPs

**Future Work:**

- Stratified Sampling Based on Patches of Interest + Extract More Samples
- Implement Weighted Aggression or Hierarchical Pooling at Slide-Level
- Perform Dimensionality Reduction (PCA, t-SNE) Prior to UMAP Plotting

# Acknowledgements

# Questions?