Predicting Mutated Genes in Multiple Myeloma from Blood-Smear Whole-Slide Images: An Early Exploration Model

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Introduction

- Multiple myeloma is a cancer of plasma cells that is usually diagnosed by a pathologist looking at blood or bone marrow slides under a microscope.

- Traditional approaches depend heavily on expert judgment and are time-consuming. Molecular tests such as NGS (accurate but costly and slow), FISH and PCR (limited to known mutations) are widely used, but remain resource-intensive and inaccessible in many settings.

- Modern deep learning methods may provide automated support by detecting abnormal regions directly from whole-slide images (WSIs).

- This study explores whether a convolutional neural network (CNN) can be trained to predict mutated regions in annotated WSIs of blood smears.

Methods

Dataset: Tissue images with binary annotations (background vs. myeloma).

**Preprocessing:** Images resize to 512x512 px; masks binarized into 0/1.

Model: Lightweight U-Net CNN ("Tiny U-Net")

Training Setup:

- 80/20 train–validation split
- Batch size: 2
- Adam optimizer (A training rule that automatically adjusts the size of each weight by running averages of recent batches)
- Loss Function:
  A score the model tries to minimize. The lower is better.
- Best models are selected by lowest validation loss

Evaluation: Pixel precision, recall, F1-score, ROC AUC, and confusion matrix.

Display: RGB tissue image shown alongside black-and-white ground truth and predicted masks.
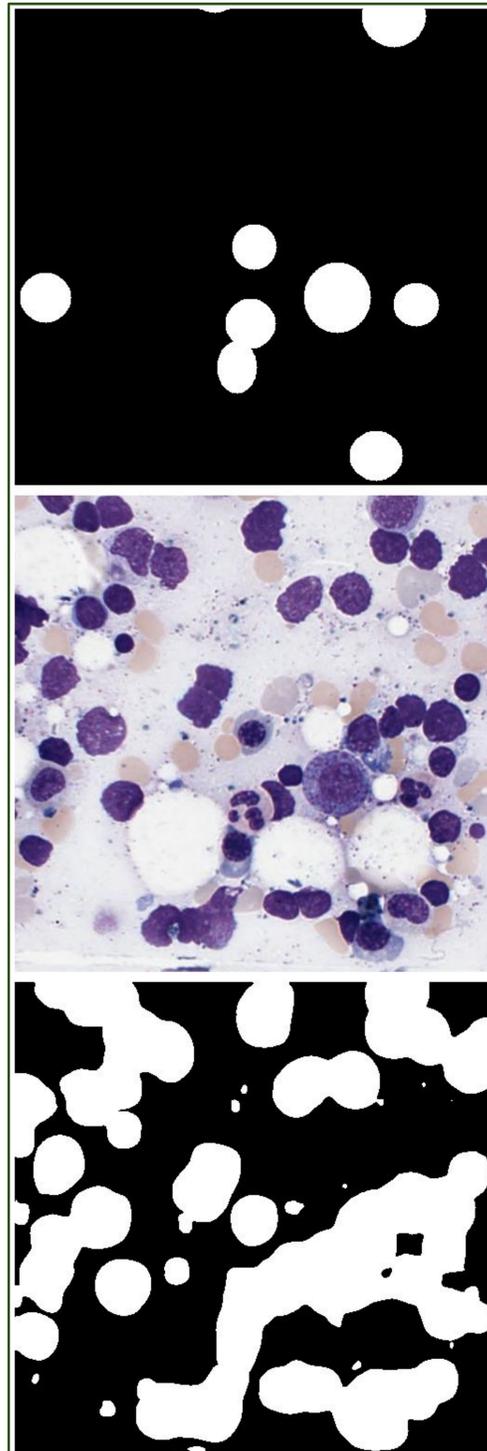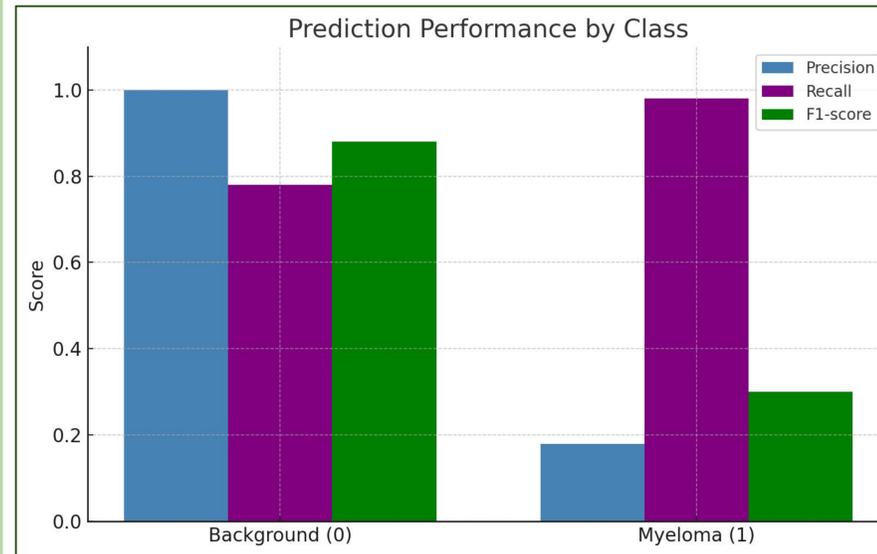
Results

Figure 1. Segmentation masks over a blood smear image.

Top: Annotated myeloma regions (white masks).

Middle: Original blood smear image with plasma cells.

Bottom: Areas the CNN identified as possible myeloma cells.

Figure 2. Classification performance metrics.

The CNN achieved 79% overall accuracy and a ROC AUC of 0.92, showing strong separation between background and myeloma. Recall for myeloma was very high (0.98), meaning the model detected most true cases. However, precision was low (0.18), indicating frequent false positives.
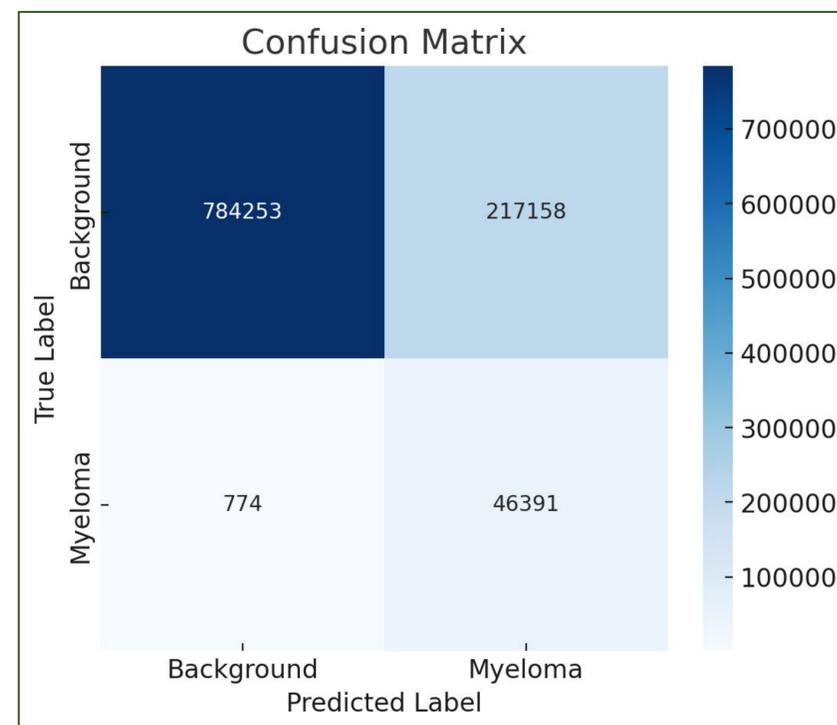
Figure 3. Confusion matrix of predictions.

- True negatives (background correctly identified): 784,253
- False positives (background misclassified as myeloma): 217,158
- False negatives (missed myeloma regions): 774
- True positives (myeloma correctly detected): 46,391

Discussion

- The model showed strong recall (0.98), detecting nearly all myeloma regions.
- However, precision was low (0.18), with many background regions misclassified as diseased tissue.
- This indicates the model has a high false-positive rate.
- A big challenge was severe class imbalance: ~1,000,000 background pixels vs. ~47,000 myeloma pixels.
- Despite these issues, the model achieved a ROC AUC of 0.92, showing strong class separation ability.
- These findings highlight the need for class balancing strategies and potentially stronger CNN architectures to improve precision.
- The model shows promise as a support tool for pathologists, helping flag suspicious areas in WSIs and speeding diagnosis.

Conclusion

- The CNN model demonstrates promising potential for assisting in multiple myeloma diagnosis from WSIs.
- Achieved high recall in detecting myeloma regions, making it effective at flagging most true cases.
- Automated analysis can highlight abnormal regions, allowing pathologists to focus on the most relevant areas instead of manually scanning thousands of cells.
- With further improvements — such as better class balance, stronger architectures, and optimized training — CNN-based models could be integrated into clinical practice.
- Ultimately, this approach may enable low-cost, scalable diagnostic support, especially valuable in low-resource settings where NGS and other molecular tests are less accessible.