

Inferring PDL-1 status from H&E images using digital pathology to identify patients responsive to anti-PD(L)-1 immuno-oncology (IO) therapy for bladder cancer trials.

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¹Janssen R&D, LLC, a Johnson & Johnson Company



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Inferring PDL-1 Status from H&E Images Using Digital Pathology to Identify Patients Responsive to Anti-PD(L)-1 Immuno-Oncology (IO) Therapy for Bladder Cancer Trials

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KEY TAKEAWAYS



We developed **MIA:PDL1**, an AI algorithm to infer PDL-1 expression from routine **H&E** images and rapidly assess the **likelihood of a patient responding to anti PD(L)-1 therapies**

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CONCLUSIONS

- ✔ We leveraged a pretrained **Foundation Model** and finetuned it to predict **PDL-1** expression from routine **H&E** images to demonstrate the algorithm's potential use for selecting patients likely to respond to **anti-PDL-1 immunotherapy**.
- ✔ We show that the model achieves a **strong performance** at classifying PDL1 status and proficiency in inferring outcomes to PDL-1 therapy in a small bladder cancer data set.
- ✔ The algorithm represents a novel approach to rapidly and accurately **assess the likelihood that a patient will respond to PDL-1 therapies** from common **H&E**-stained images. More validation is warranted to establish the power of this model to guide treatment.

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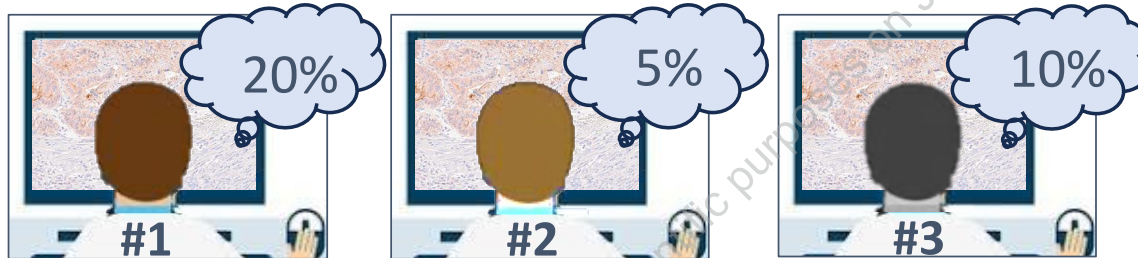


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INTRODUCTION

- Targeted IO therapies are available to **inhibit the PDL-1 pathway** and improve therapeutic response.
- Immunohistochemistry (IHC) testing is used to **assess PDL-1 expression** and guide IO therapy, but an alternative is warranted on **limited tumor samples** and to avoid **pathologist subjectivity**.



- We developed **MIA:PD11**, an AI algorithm to **infer PDL-1 expression from routine H&E images** and identify patients that may respond to IO therapies

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- Pretrained a **Foundation Model (FM)** using **~55k** whole slide images (WSIs) from various data sources (multiple scanners, hospitals/labs, diseases, tissue types).
- Fine-tuned the pretrained model on **1546 WSIs with PDL-1 labels** from corresponding IHC stained tissues, where appropriate thresholds for various included antibodies were used:
 - **PDL1-High:** TPS \geq 10% (22C3), CPS \geq 10% (22C3), CPS \geq 1% (28-8), IC \geq 5% (SP142), IC \geq 1% (SP263, LDT)
- We evaluated the **performance at predicting PDL1-High vs. PDL1-Low**, quantified by the Area Under ROC Curve (**auROC**) on a holdout set (n=388) and an independent set (n=93)
- Then, we applied the model to WSIs of **biopsies taken prior to anti-PDL-1 treatment** (i.e., pembrolizumab) and **evaluated treatment response** for the two groups (PDL1-High vs. PDL1-Low)
- We compared it to patients stratified based on IHC-based pathology readouts using the thresholds for corresponding antibodies (TPS \geq 10% vs. TPS $<$ 10%)

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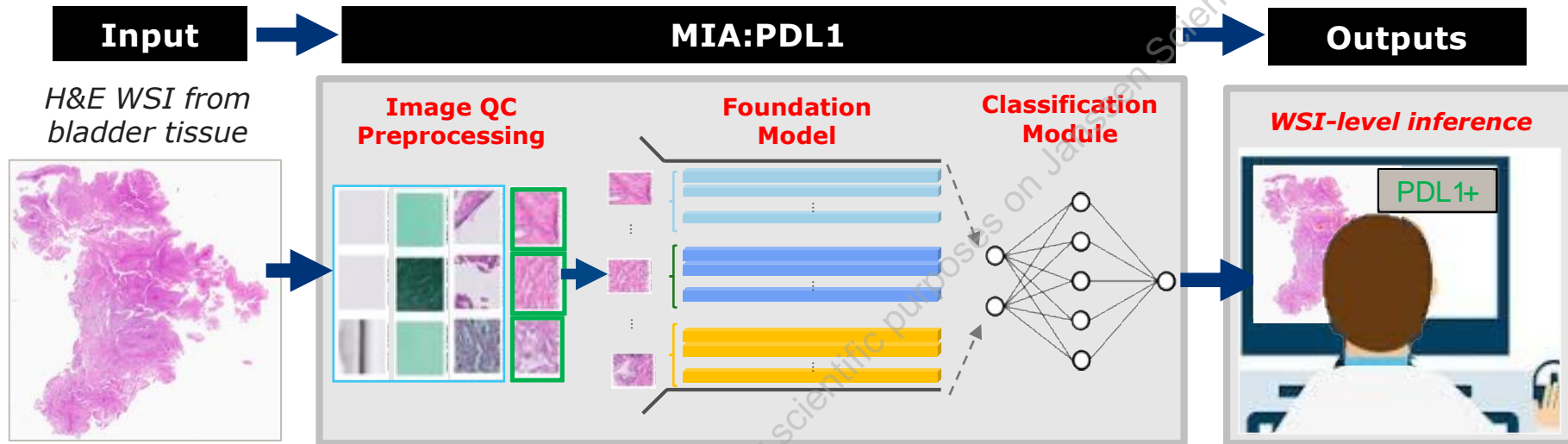
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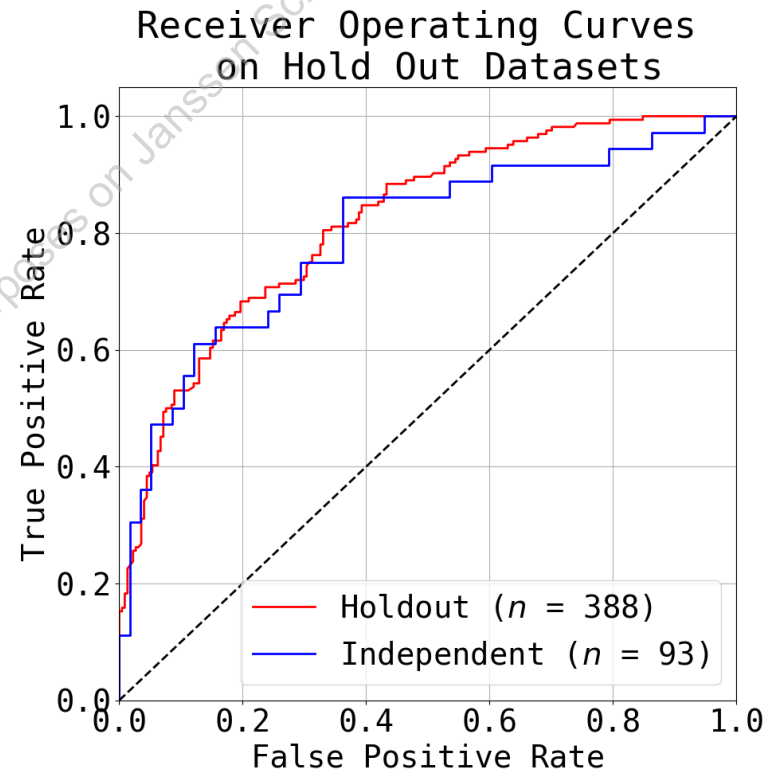
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RESULTS

- We evaluated the performance at **predicting PDL1-High vs. PDL1-Low**, quantified by the Area Under ROC Curve (**auROC**) on:

- a holdout set (n=388): **auROC=0.82**
- an independent set (n=93): **auROC=0.80**



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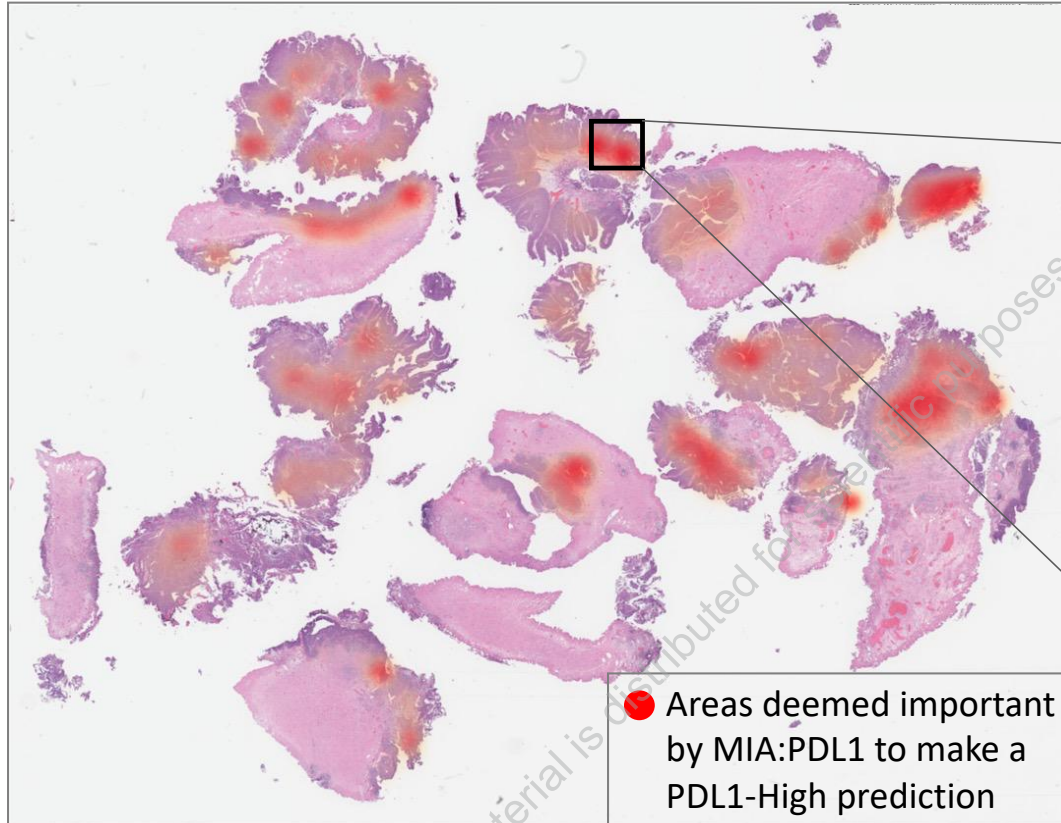


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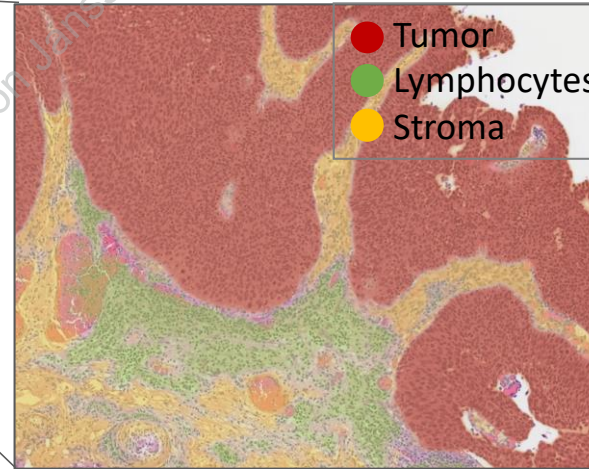
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MIA:PDL1 Output Heatmap



Tissue types in area of high importance



These tissue regions were generated by an algorithm that leverages the same Foundation Model as MIA:PDL1

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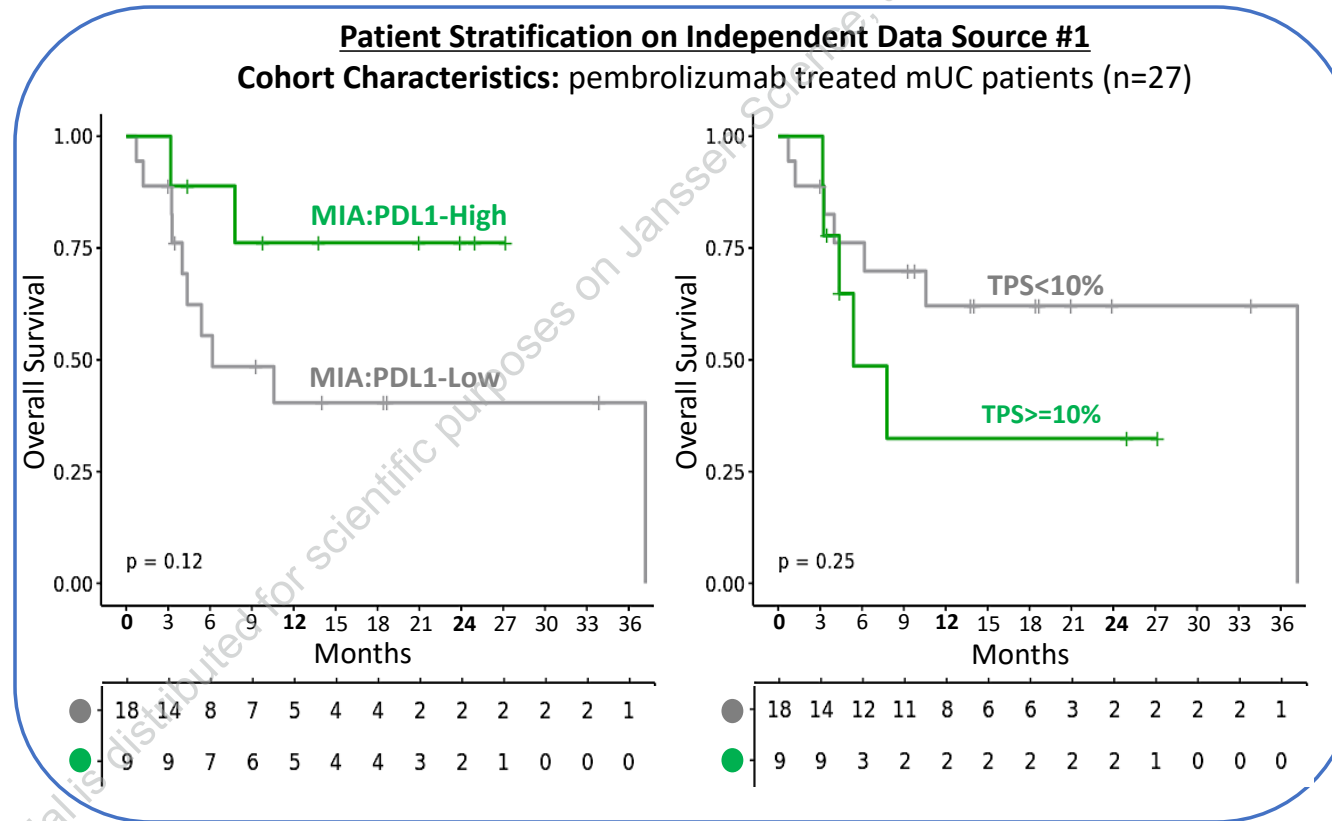


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- The figure shows the **survival analysis** results upon **pembrolizumab** treatment (n=27) when stratifying patients using MIA:PDL1 (left) vs. IHC-based readouts (right)
- Note that the survival probability for **MIA:PDL1-High** patients is higher than **MIA:PDL1-Low** patients, as opposed to IHC-based stratification.



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