Poster #1030

# AI-Driven Microsatellite Instability Testing in Gastric and Endometrial Cancers: towards full reflex testing

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## Background

- Microsatellite instability (MSI) testing is crucial for managing solid tumor patients, particularly for immune checkpoint inhibitor therapy. [2]
- Reflex MSI testing is recommended for colorectal cancer (CRC), gastric cancer (GC), and endometrial cancer (EC), but challenges such as workload, cost, and tissue availability result in underdiagnosis.
- While AI models were developed for MSI testing in CRC, limited work exists for **less prevalent cancers** like GC and EC.

## Objectives

- Develop AI models for MSI testing in GC and EC with strong validation performance despite low prevalence and limited access to data.

## Results

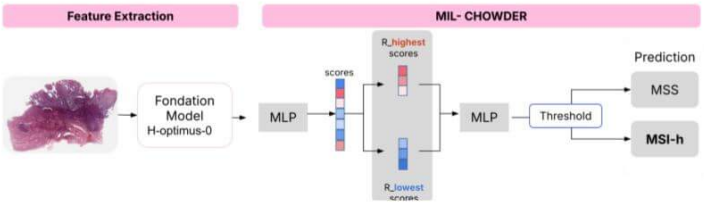
- **GC**: The model achieved an average AUROC of 0.934 (0.916, 0.935, 0.950) for three left-out cohorts.
- **EC**: The model achieved an average AUROC of 0.830 (0.774, 0.820, 0.895) for three left-out cohorts.

**Table: cross-validation performance**. *CIs are adjusted for the cross-validation with Nadeau & Bengio's corrected t-test.*

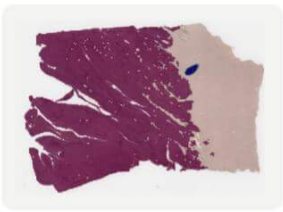
| Model | Training | Evaluation | Cross-validation AUROC | Specificity at 80% Sensitivity |
|---|---|---|---|---|
| Gastric locked model | TCGA-STAD, VHIR, ZNA-GZA | TCGA-STAD | 0.922 (0.865, 0.980) | 0.902 (0.844, 0.960) |
| | | VHIR | 0.947 (0.907, 0.987) | 0.922 (0.861, 0.983) |
| | | ZNA-GZA | 0.944 (0.894, 0.996) | 0.904 (0.805, 1.000) |
| ***Aggregated mean (std) over cohorts*** | | | ***0.938 (0.011)*** | ***0.909 (0.009)*** |
| Endometrial locked model | TCGA-UCEC GR, ZNA-GZA | TCGA-UCEC | 0.810 (0.755, 0.867) | 0.667 (0.575, 0.758) |
| | | ZNA-GZA | 0.780 (0.666, 0.894) | 0.626 (0.442, 0.811) |
| | | GR | 0.908 (0.844, 0.973) | 0.854 (0.709, 0.998) |
| ***Aggregated mean (std) over cohorts*** | | | ***0.833 (0.055)*** | ***0.716 (0.099)*** |

## Method

- **Task**: Predict MSI status from digitized H&E slides in GC and EC
- **Model**: Foundation Model (H-optimus-0 [1]) + MIL (Chowder)




- **Tumor Filtering :** In EC, non-tumor regions were automatically excluded during training



- **Evaluation Method**: A "leave-one-cohort-out" validation approach was used to ensure generalizability and minimize overfitting.

## Data

- **Data**: independent multi-center cohorts (4 proprietary, 2 per indication, from 3 countries, N=556 patients; TCGA, N=851 patients).

| Indication | Cohort | N. patients (MSI-h) | N WSI | Tissue type |
|---|---|---|---|---|
| GC | TCGA-STAD | 373 (63) | 399 | Resections |
| GC | ZNA-GZA | 111 (14) | 111 | Biopsies |
| GC | VHIR | 206 (36) | 210 | Resections + biopsies |
| EC | TCGA-UCEC | 478 (153) | 559 | Resections |
| EC | ZNA-GZA | 130 (41) | 216 | Resections + biopsies |
| EC | GR | 109 (41) | 109 | Resections |

## Discussion

- Our AI models for MSI detection in GC and EC demonstrated strong validation performance. The "leave-one-cohort-out" strategy was crucial in ensuring robust generalization for future external validation and clinical use. These models hold promise of delivering faster, cost-effective solutions, advancing toward routine reflex MSI testing for GC and EC.

## References & acknowledgements

[1] Saillard, C., Jenatton, R., Llinares-López, F., Mariet, Z., Cahané, D., Durand, E., Vert, J.P.: H-optimus-0 (2024), https://github.com/bioptimus/releases/tree/ main/models/h-optimus/v0

[2] Kavun, Alexandra, Egor Veselovsky, Alexandra Lebedeva, Ekaterina Belova, Olesya Kuznetsova, Valentina Yakushina, Tatiana Grigoreva, Vladislav Mileyko, Mikhail Fedyanin, and Maxim Ivanov. 2023. "Microsatellite Instability: A Review of Molecular Epidemiology and Implications for Immune Checkpoint Inhibitor Therapy." Cancers 15 (8): 2288.

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