Implementation of Centralized MMR Sequencing of Colorectal Cancer Specimens Increases Genetic Screening Efficacy

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Introduction

- 15% of all patients with colon and rectal cancer (CRC) have a pathogenic variant germline mutation
- Most notable are the germline mutations associated with Lynch Syndrome (LS)[1]
- The National Comprehensive Cancer Network (NCCN) recommends universal screening for LS for all CRC
  - Mismatch repair (MMR) or microsatellite instability (MSI)
  - Aim to increase genetic testing in those at increased risk.[3]
- At our institution, MMR/MSI testing of CRC remains suboptimal.

This study aims to:

1. **Assess the impact of in-house MMR sequencing on LS screening compliance**
2. **Evaluate the impact of this change on rates of germline testing for LS**

Methods

- Single-institution retrospective cohort analysis
- Patients age >18 with diagnosis of CRC between **January 2022 and November 2023**

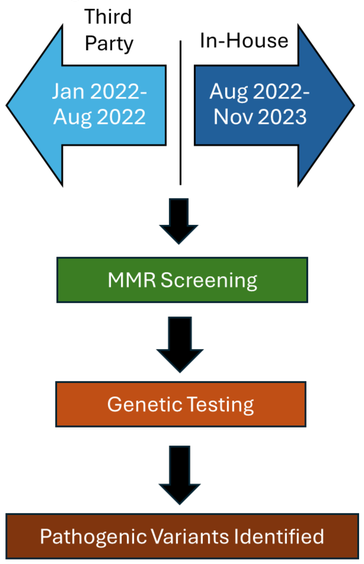

Figure 1. Patients from the cohort analysis were divided into two groups based on whether they received testing before vs after the change from third party to in-house testing, with statistical significance for primary and secondary outcomes calculated with a Z-score.

- Primary outcome: MMR screening efficacy
- Secondary outcomes: Genetic testing rate, frequency of pathogenic genetic variants

Results

324 patients were identified, with **87 patients** who received tumor sample MMR testing from **a third party** and **217 patients** who received **in-house** testing

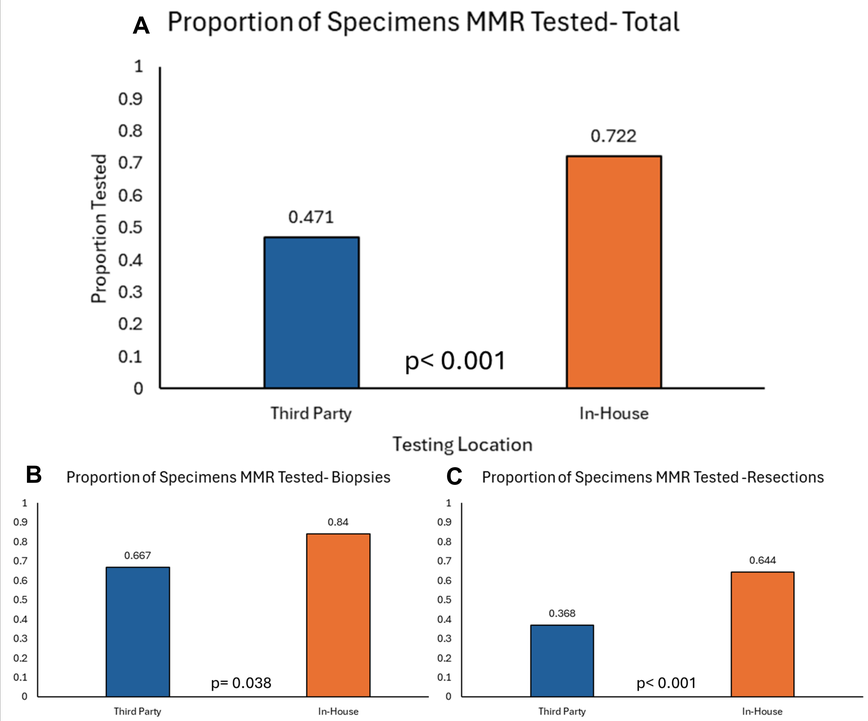

Figure 2. Overall, a significant increase in MMR testing efficacy was seen in those who received in-house testing versus from a third party **(A)**. This remains true whether the samples tested were biopsied specimens **(B)** or surgical resections **(C)**.

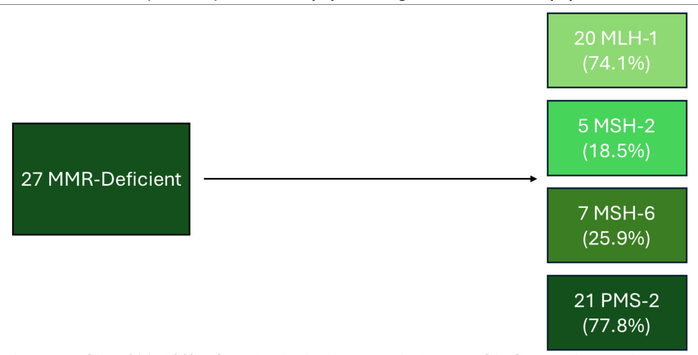

Figure 3. A total of 27 (11.4%) of patients in this study had a CRC specimen that was determined to have an MMR deficiency. Rates of pathogenic variants as determined by MMR testing are shown.

References

1. Benson, et al. (2021). doi: 10.6004/jnccn.2021.0012.
2. Stoffel, et al. (2018). Doi: 10.1053/j.gastro.2017.11.004

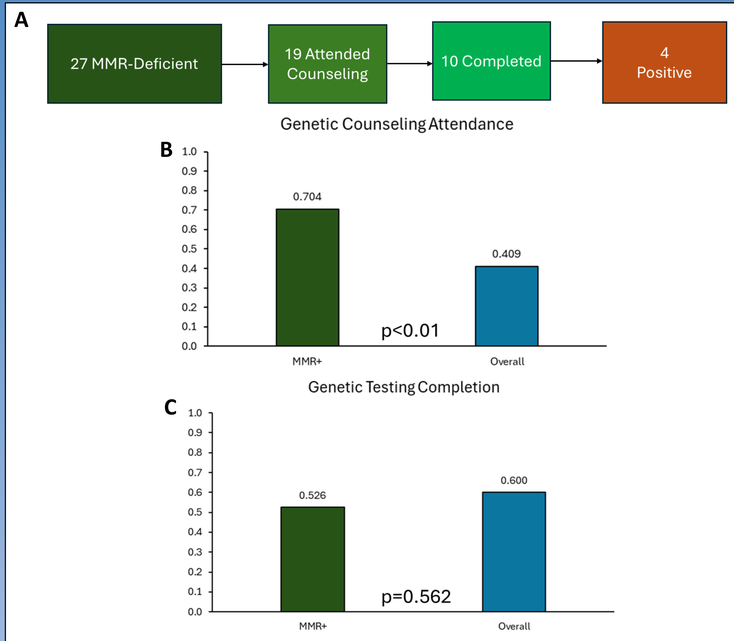

Figure 4. Of those identified as MMR-deficient, a breakdown of those who attended genetic counseling, completed genetic testing, and those who tested positive for germline mutations **(A)**.Prior to the implementation of genetic counseling into a multidisciplinary tumor clinic, those with MMR-deficient tumors were more likely to attend genetic counseling **(B)**, though this did not translate to increased genetic testing rates **(C)**.

Conclusions

- The efficacy of in-house MMR testing of colon and rectal tumors is significantly superior to that of third-party testing
- Most patients with identified MMR variants are appropriately referred to genetic counseling
- The lack of translation to genetic testing highlights additional barriers to germline testing for CRC

Future Directions

- Investigate impact of integration of genetic counselors into a multidisciplinary tumor clinic on NCCN guideline-concordant genetic testing rates
- Further quality improvement investigation to increase in-house MMR deficiency testing in order to work toward NCCN guideline-compliant universal testing