

 <p><b>UniSR</b> Università Vita-Salute San Raffaele</p>	<p><b>APPLICATION TO ACT AS SUPERVISOR AND RESEARCH PROJECT PROPOSAL</b></p>	<p><b>MO 20-5</b> ed. 01 del 21/02/2025 PO 20 Page 4 of 11</p>
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**PROJECT**

**Supervisor:** Giulia Martina Cavestro

**Title:** Liquid biopsy and machine learning for early colorectal cancer, adenomas, Lynch cancers, and residual disease detection

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**Description of the Project (max 3,000 characters including spaces)**

**Background/gap of knowledge**

Colorectal cancer (CRC) remains a significant public health burden despite being potentially preventable. Current screening modalities, such as fecal immunochemical tests (FIT) and colonoscopy, have limitations. FIT exhibits reduced sensitivity for early-stage CRC and precursor lesions (advanced adenomas, AAs), while colonoscopy presents challenges related to invasiveness, cost, and patient compliance. Non-invasive blood-based tests offer a promising alternative but have demonstrated suboptimal sensitivity for AAs and early-stage CRC.

Individuals with Lynch syndrome (LS) have a germline defect in one of the four mismatch repair (MMR) genes that predisposes them to several cancers. Multi-cancer early detection (MCED) has emerged as a promising field (e.g., Grail and CancerGuard blood-based assays). Yet, their application remains largely unexplored in LS and the existing commercial assays may not be optimally suited for early detection in these high-risk populations.

**Rationale and hypothesis**

We hypothesize that CRC screening programs may be complemented by a sensitive, non-invasive, inexpensive, and easily repeatable blood-based test and that LS surveillance programs may benefit for an ad-hoc developed MCED test.

**Objectives and specific aims**

We propose a develop and validate two blood-based tests: one that is sensitive to CRC and AA and specific to complement CRC screening options, and another MCED test that is sensitive to LS-spectrum tumors and specific to complement LS surveillance options

**Expected outcomes**

In our two proposed aims, grounded in circulating microRNAs and the subsequent development of comprehensive miRNA panels, we plan to address two critical clinical gaps: first, the development of a blood-based test that is sensitive to both AA and CRC, and second, an MCED



test that proves to be cheap, and convenient for patients with LS, while also providing clinicians with sensitivity and specificity.

**Skills that the student should acquire** (max. 600 characters including spaces):

- Help design, plan, and conduct basic and translational research projects
- Participate in the development and validation of liquid biopsy-based biomarkers
- Analyze and interpret biological and clinical datasets using statistical methods and bioinformatics tools
- Collaborate with other team members and external partners, including clinicians, statisticians, and computational biologists
- Contribution on scientific manuscripts/research grants writing
- Participate in the development of machine learning models for biomarker discovery and predictive analytics under the supervision of senior researchers.

**References** (max. 15)

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13. Matsuyama T, Toiyama Y, Ishikawa T, et al. A metastasis-associated microRNA-based liquid biopsy signature for risk-stratification in colorectal cancer: a multicenter cohort study. *Clin Transl Med*. Dec 2022;12(12):e998. doi:10.1002/ctm2.998
14. Nakamura K, Hernandez G, Sharma GG, et al. A Liquid Biopsy Signature for the Detection of Patients With Early-Onset Colorectal Cancer. *Gastroenterology*. Nov 2022;163(5):1242-1251e2.doi:10.1053/j.gastro.2022.06.089
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