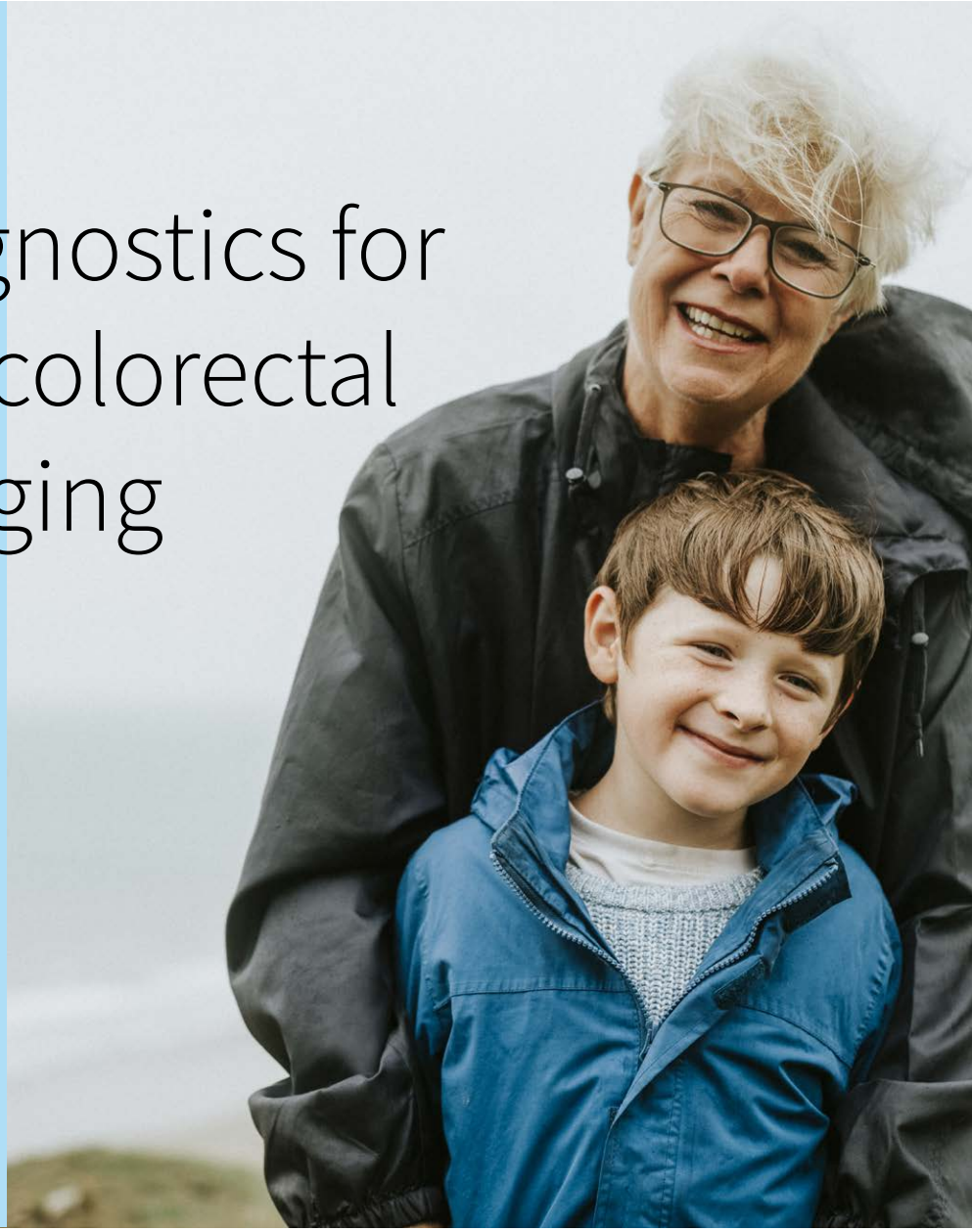
colonode®

Novel Diagnostics for improved colorectal cancer staging



Reaching beyond histopathology by using molecular biomarkers

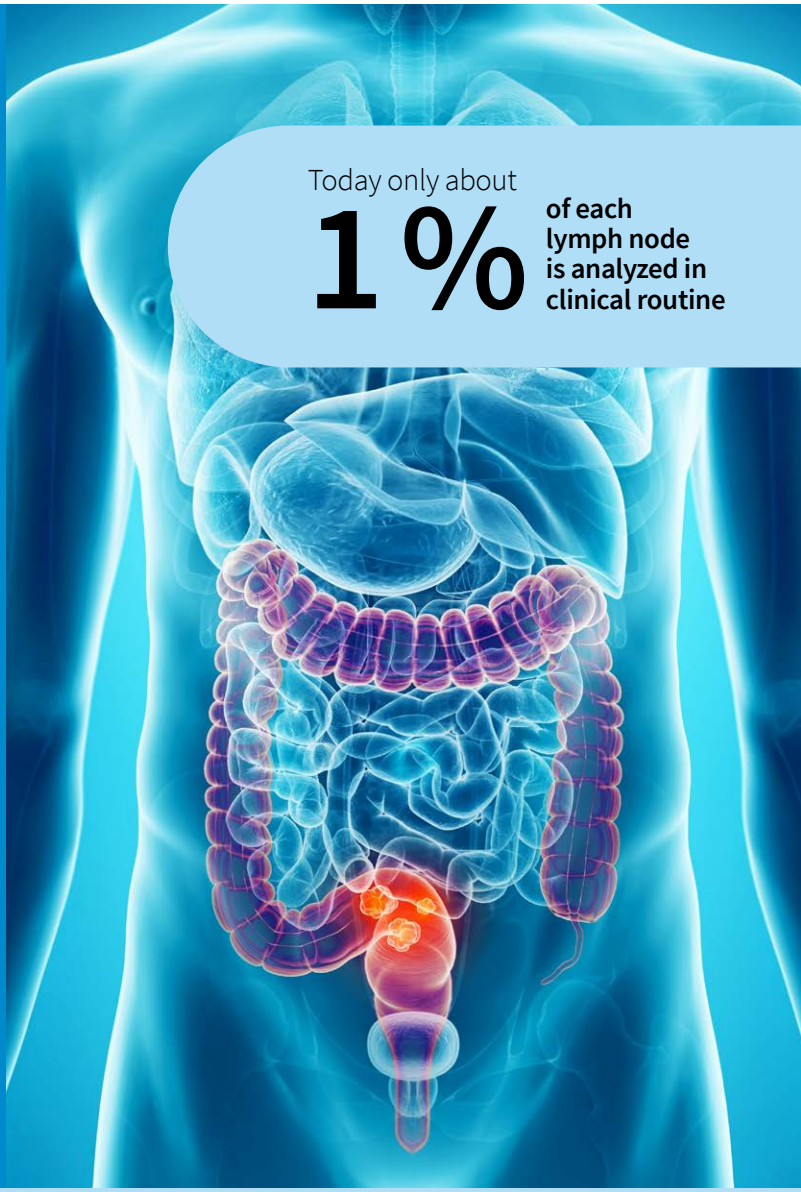
With current diagnostics, a fourth of colorectal cancer patients judged to be cured by surgery will die from tumor recurrence

How can we reduce recurrence rates and increase survival?

Lymph nodes are key elements of the TNM (Tumor, Node and Metastasis) staging System. The presence or absence of disseminated tumor cells is the single most important factor when predicting disease-free survival and overall survival for patients with colorectal cancer without distant metastasis. The lymph node status is also a crucial factor when deciding on adjuvant chemotherapy treatment after curative surgery.

However, today only about 1 % of each lymph node is analyzed in clinical routine.

ColoNode® is a novel In Vitro Diagnostics for colorectal cancer that detects and characterizes tumor cells in lymph nodes by measuring mRNA levels of five biomarkers. In addition, ColoNode® estimates the risk of tumor recurrence based on the expression profile of these biomarkers. The ColoNode® can analyze up to 100% of the lymph node volume. This provides an increased basis for decision-making in staging and decisions on adjuvant chemotherapy treatment and follow-up.

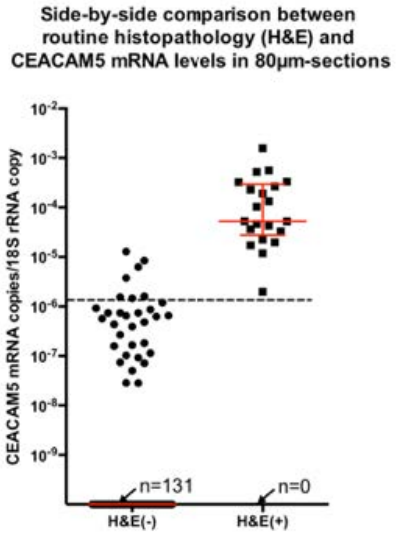


ColoNode®

ColoNode® is a multiplex qRT-PCR assay that analyzes the mRNA levels of five biomarkers and one control gene in 20 individual lymph node samples:

- CEACAM5 protein is a well-established tumor marker in colorectal cancer. CEACAM5 mRNA levels correlate well with the number of tumor cells and high levels correlate to poor prognosis[1,2]
- Expression of KLK6 mRNA is associated with poor prognosis[3]
- Expression of SLC35D3 mRNA is associated with poor prognosis[4]
- High levels of stromal POSTN mRNA correlate to poor prognosis[4]
- Lymph nodes harboring tumor cells with high levels of MUC2 mRNA is an indicator of good prognosis[2]

Scientific results



ColoNode® increases detection of metastases/micrometastases 1.33-fold compared to histopathology (H&E)

This figure shows the results from side-by-side analysis of 185 lymph nodes comparing histopathology (H&E) and CEACAM5 levels by ColoNode.

All H&E-positive lymph nodes have high CEACAM5 levels. Notably, 7 H&E-negative lymph nodes have as high CEACAM5 levels, thus harboring similar amounts of tumor cells as H&E-positive nodes but missed by histopathology. The CEACAM5 levels of these lymph nodes and the H&E-positive nodes are all higher than the "clinical cut-off" above which there is an increased risk of recurrence.[5]

Additional 26 lymph nodes have detectable CEACAM5 mRNA just below the clinical cut off, meaning no micrometastasis but still isolated tumor cells.

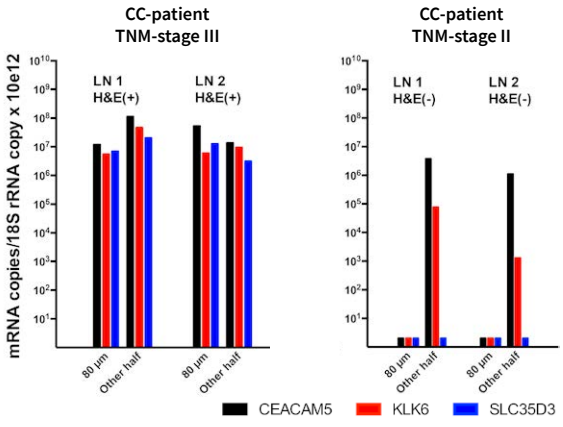
References 2 and 5

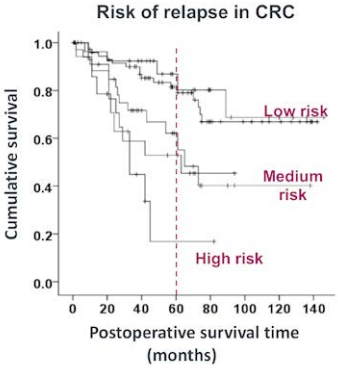
Increasing the amount of tissue analyzed improves detection

Examples from ColoNode analyses of RNA extracts of one 80 µm section compared to half the lymph node.

High levels of CEACAM5 and aggressiveness markers KLK6 and SLC35D3 were seen in both 80 µm sections and half nodes in 4 lymph nodes that had a metastase according to histopathology [=H&E(+)]. In H&E- lymph nodes however, it was critical to analyze half the lymph node to detect CEACAM5, KLK6 and SLC35D3 at significant levels.

Reference 5





Risk categorizing of patients based on aggressiveness markers

Based on the aggressiveness markers in ColoNode® – there is a possibility to allocate patients to three categories with different risk for recurrence. These risk categories proved to be prognostic factors independent of TNM-stage and tumor grade, which could support decisions on adjuvant chemotherapy and follow-up.

Reference 4

References

1. Öberg Å, Lindmark G, Israelsson A, Hammarström S, Hammarström M-L. Detection of occult tumor cells in lymph nodes of colorectal cancer patients using real-time quantitative RT-PCR for CEA and CK20 mRNAs. Int J Cancer. 2004;111:101-110. doi: 10.1002/ijc.20231. PMID: 15185350.
2. Ohlsson L, Israelsson A, Öberg Å, Palmqvist R, Stenlund H, Hammarström M-L, Hammarström S, Lindmark G. Lymph node CEA and MUC2 mRNA as useful predictors of outcome in colorectal cancer. Int J Cancer. 2012;130:1833-1843. doi: 10.1002/ijc.26182. PMID: 21618511.
3. Ohlsson L, Lindmark G, Israelsson A, Palmqvist R, Öberg Å, Hammarström M-L, Hammarström S. Lymph node tissue kallikrein-related peptidase 6 mRNA – a progression marker for colorectal cancer. Br J Cancer. 2012;107:150-157. doi: 10.1038/bjc.2012.220. PMID: 22699826.
4. Olsson L, Hammarström M-L, Israelsson A, Lindmark G, Hammarström S. Allocating colorectal cancer patients to different risk categories by using a five-biomarker mRNA combination in lymph node analysis. PLoS ONE. 2020;15:e0229007. doi: 10.1371/journal.pone.0229007. eCollection 2020. PMID: 32049988.
5. Olsson LM, Lindmark GE, Israelsson ACE, Korkocic D, Hammarström SG, Hammarström M-LKC. CEACAM5, KLK6, SLC35D3, POSTN and MUC2 mRNA analysis improves detection and allows characterization of tumor cells in lymph nodes of colon cancer patients. Dis Colon Rectum. 2021;64:1354-1363. doi: 10.1097/DCR.0000000000002151. PMID: 34192710.

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