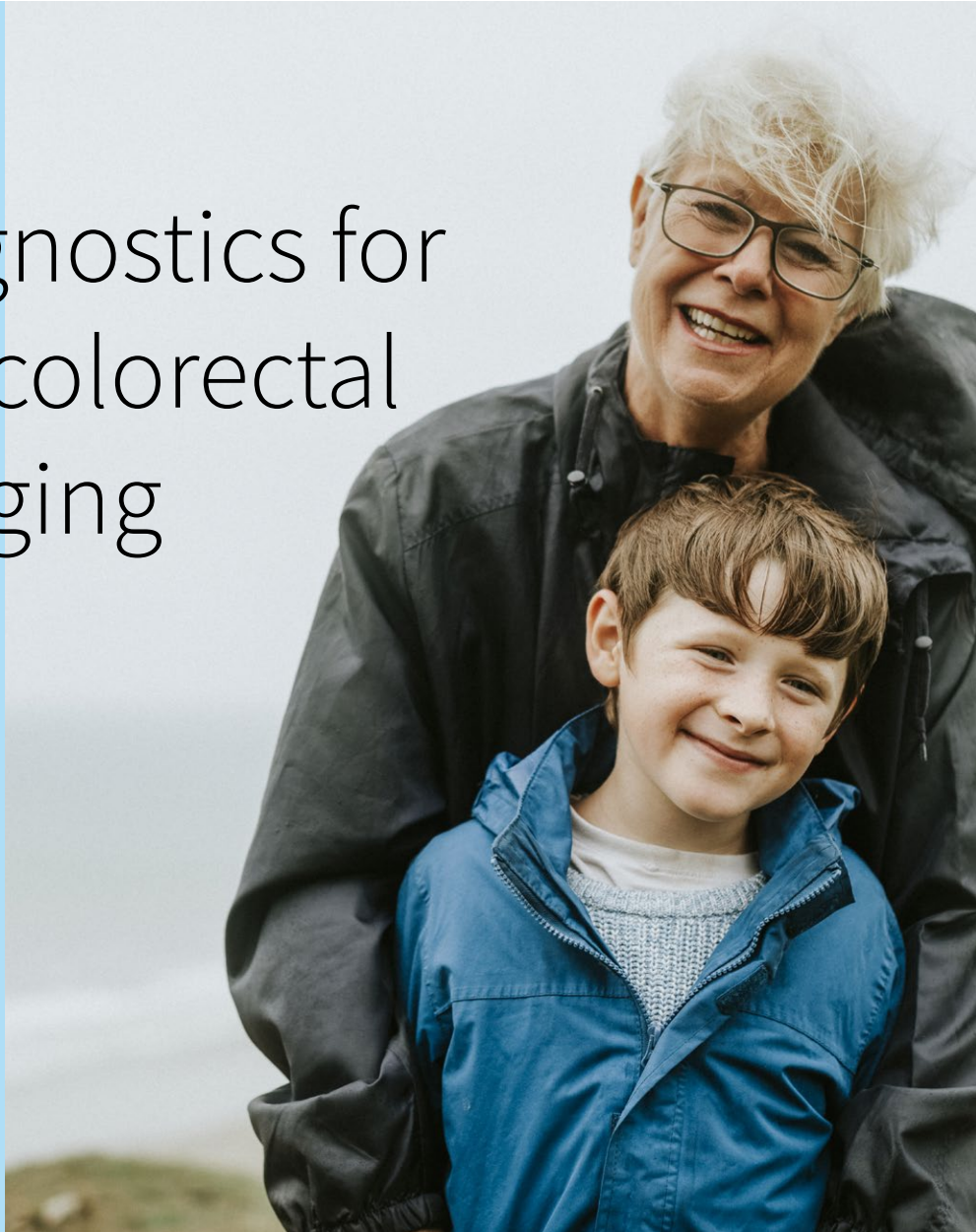# colonode®

Novel Diagnostics for improved colorectal cancer staging

Reaching beyond histopathology by using molecular biomarkers

With current diagnostics, one 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. ColoNode® estimates the risk of tumor recurrence based on the expression profile of these biomarkers. 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.

Today only about

1 %

**of each lymph node is analyzed in clinical routine**

ColoNode®

ColoNode® is a multiplex qRT-PCR assay that analyzes the mRNA levels of five biomarkers and one control gene:

- CEACAM5 protein is a well-established tumor marker in colorectal cancer. CEACAM5 mRNA levels correlate strongly with the number of tumor cells[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]
- ColoNode gives an estimate of risk of recurrence and allocates the patient to one of four risk groups[6]

Most important scientific results
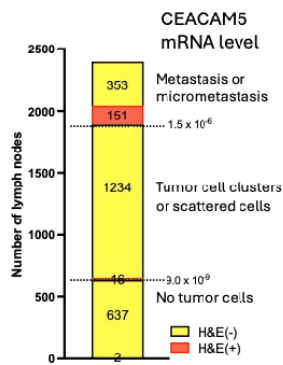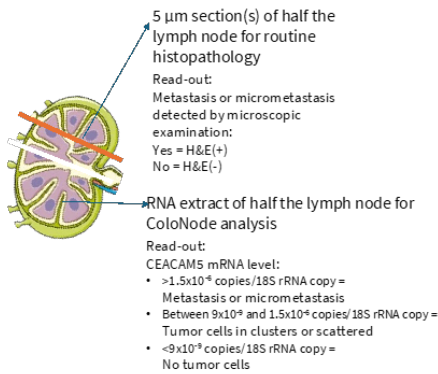
ColoNode is superior to histopathology for detection of tumor cells in lymph nodes

Histopathology (H&E) and CEACAM5 mRNA level by ColoNode were compared for detection of tumor cells in 2393 lymph nodes of 196 colon cancer patients.

ColoNode **increased detection of metastases and micrometastases 3.34-fold** compared to histopathology.

73% of the lymph nodes were CEACAM5-positive, that is, harbored tumor cells.
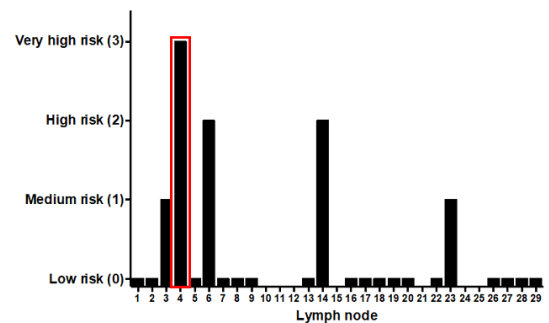
References 5 and 6

Allocation to risk groups by ColoNode

For each CEACAM5-positive lymph node a risk factor is calculated by a formula for the expression of biomarkers KLK6, SLC35D3, POSTN and MUC2.

(-1) and (0) = low risk   (1) = medium risk
(2) = high risk   (3) = very high risk

The lymph node with the highest risk factor defines the risk group to which the patient is allocated

ColoNode surpasses histopathology in identifying patients at risk of recurrence

The COLONODE-study – a prospective multicenter study in which all lymph nodes examined by histopathology in the clinic also were analyzed by ColoNode. Lymph nodes were from 196 colon cancer patients receiving curative surgery. At 3-year follow-up 36 patients had died from their cancer or lived with recurrent disease.
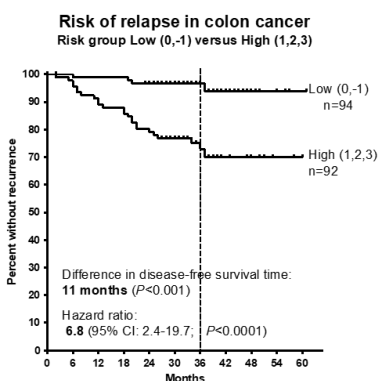
COLONODE RISK GROUP 1 OR HIGHER (1,2,3):

- identified **all** patients who had recurred that were identified by histopathology (21 patients; 58%)

- identified **9 additional** patients who had recurred **(25%, P < 0.0001)**

- proved to be a highly significant, independent risk factor with a **hazard ratio of 4.24** (95% CI, 1.42-12.69; P = 0.01) in **multivariate analysis**, while histopathology (pTN-stage III vs I/II) lost its univariate significance

PATIENTS IN COLONODE RISK GROUP LOW (0,-1), = 51%:

- have very low risk of recurrence, that is, these patients **are likely cured by surgery alone**

- PATIENTS IN COLONODE RISK GROUP HIGH/VERY HIGH (2,3), = 29%:

- are at high risk of recurrence with a hazard ratio of 10.6 (95% CI: 3.6-31.2) compared to the Low (0,-1) group. These patients **are likely to benefit from postoperative adjuvant treatment**

Reference 6

References

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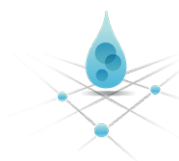
1. 2. 3. 4. 5. 6.

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HiloProbe AB, Tvistevägen 48C, 907 36 Umeå, Sweden

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