Trucheck™

Early Cancer Screening

Nordic Laboratories®

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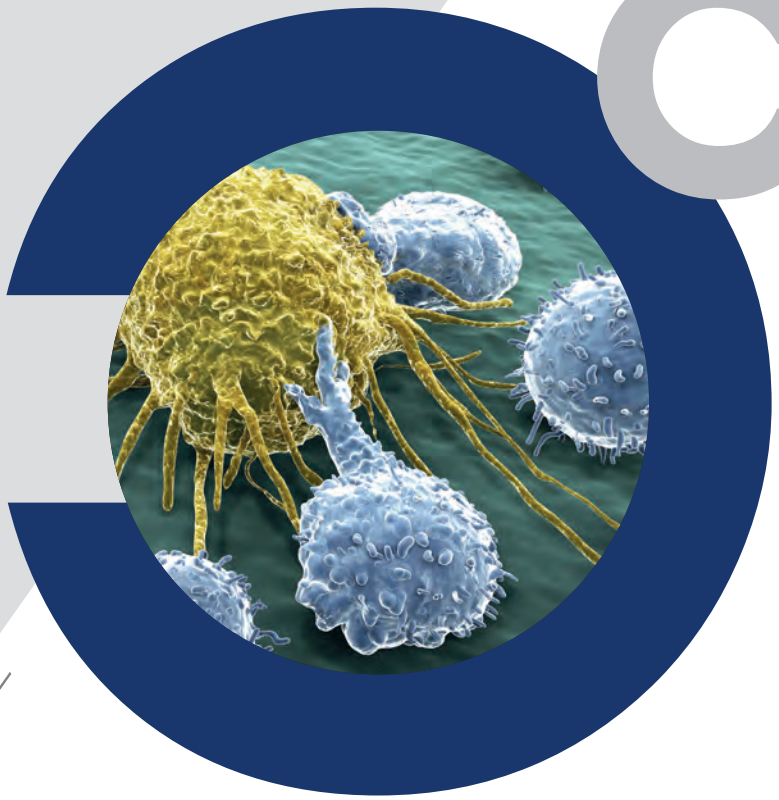


About Trucheck™

Trucheck™ is a new blood-based paradigm in multicancer detection.

About 4.4 million new cancers are detected every year in Europe as well as about 2 million cancer related deaths. Unfortunately, some cancers are detected at advanced stages which necessitate more intensive and expensive treatments which have greater risk of side effects. Detection of cancers at early / local stages is vital for successful treatments, lower treatment costs, lower toxicities and improved survival.

Trucheck™ is the culmination of years of collaborative international research and innovation and has been developed, **tested and validated on > 57.000 individuals.**

Trucheck™ is a non-invasive blood-based test to detect cancers in asymptomatic individuals.

SENSITIVITY

92.1%

SPECIFICITY

99.9%

Trucheck™ technology

- Trucheck™ detects circulating tumour cells (CTCs) and clusters of these CTCs which are released by malignant tumours, but not from non-cancerous (normal / benign tumour / inflammatory) tissue. Hence CTCs are ubiquitously seen in blood of cancer patients but absent in blood of healthy individuals.
- Trucheck™ intelli can distinguish **~70 types of solid tumours** which account for ~81% of all cancer cases and ~84% of all cancer related deaths in Europe.
- Trucheck™ has a **92.1% sensitivity** in detection of cancers across all stages and types. Further Trucheck™ intelli has a **93.1% accuracy** in determining the tissue or organ of origin in positive cases.
- Trucheck™ displays a **specificity of 99.9% (versus healthy individuals)**. Trucheck™ detects cancers irrespective of the extent of the disease, thus even early-stage cancers are reliably observed.

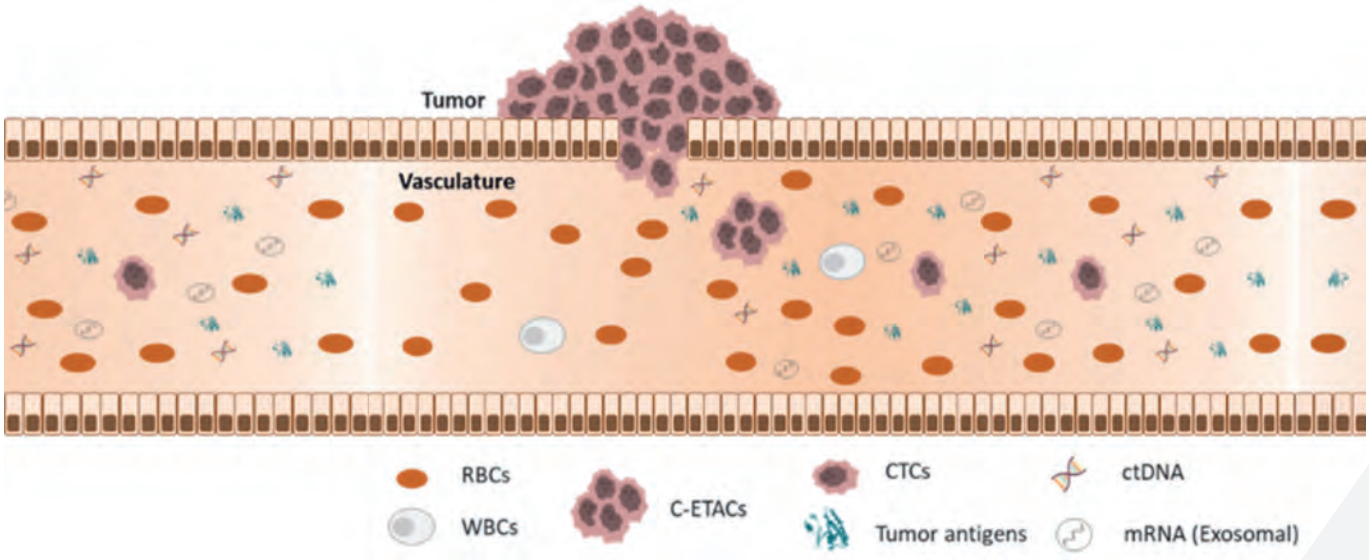
Trucheck™

Trucheck™ is particulary recommended for ...

... asymptomatic individuals who have a family history of cancer.

... individuals who want to include this test in their yearly check-up.

... asymptomatic individuals who have a high risk in cancer.



Advantages Trucheck™

- In contrast to screening for a single cancer at a time, Trucheck™ can identify multiple cancer types via a simple blood draw that may be undetectable by present technologies. Detection at earlier stages is associated with greater rates of successful treatment and improved survival.
- Trucheck™ intelli interrogates CTCs for the molecular imprint of the tumour mass from where the CTCs originated, i.e., Trucheck™ intelli reveals diagnostically relevant information about the tissue / organ of origin of the tumor with high accuracy. This guides further investigations and reduces diagnostic trial and error.
- Trucheck™ is an advanced comprehensive cancer detection that offers an unparalleled combination of sensitivity and specificity for early detection of cancers in asymptomatic individuals.

Important publications

Publication	Population			Parameters	Performance Characteristics	
	Cancers	Benign	Asymptomatic		Specificity	Sensitivity
Akolkar D. et al. Circulating ensembles of tumor-associated cells: A redoubtable new systemic hallmark of cancer. (International Journal of Cancer)	5.509 (R)	-	10.625 (P)	Analyte: C-ETACs, CTCs Proof of Concept Study	96.4% (Asymptomatic)	89.5% (Retrospective)
Renade A. et al. Hallmark Circulating Tumor-Associated Cell Clusters Signify 230 Times Higher One Year Cancer Risk. (AACR)	5.509 (R) 4.419 (P)	324 (P)	10.625 (P)	Analyte: C-ETACs, CTCs Assessment: CDA[1] Proof of Concept Follow-up Study	97.5% (Benign) 93.0% (Retrospective)	95.6% (Asymptomatic) 93.0% (Prospective)
Gaya A. et al. Evaluation of circulating tumor cell clusters for pan-cancer non-invasive diagnostic triaging. (ACS Journal)	9.416 (R) 6.025 (P)	700	13.919 (P)	Analyte: C-ETACs, CTCs Assessment: CDA Clinical Validation Study	99.3% (Benign) 85.2% (R)etrospective	100.0% (Asymptomatic) 86.7% (Prospective)

[1]Colony Detection Assay; P = Prospective, R = Retrospective

Trucheck™

Sample collection

REQUIREMENTS

Total 3 tubes containing 22 ml whole blood

- First draw 2 ml SST tube (yellow colour cap)
- Second draw 2 x EDTA tubes (purple colour cap) of 10 ml each - total 20 ml

NOTE
Sequence of draw should not be altered.
Blood drawn should be performed only be qualified phlebotomist under medical supervision.
Ship at 4 °C in the container provided by DCG.

PRECAUTIONS

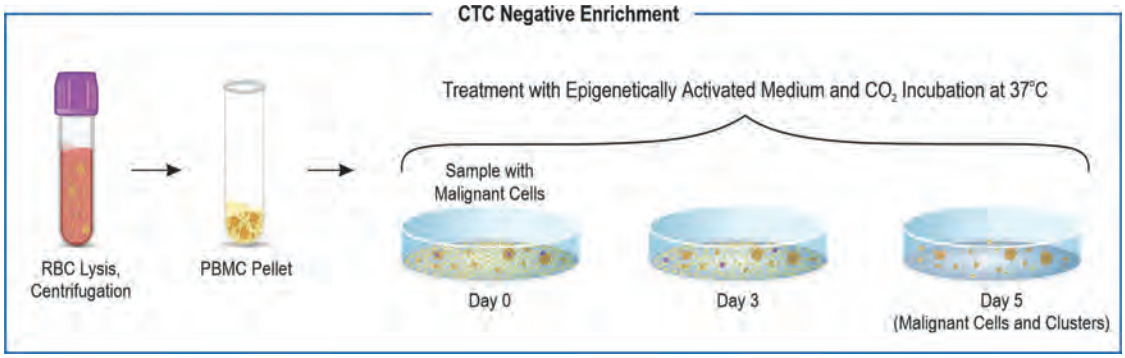
- Patient has not received blood transfusion at least 10 days prior to collection of sample.
- Patient is not positive for HIV / HBV / HCV.

Method

CTC enrichment:

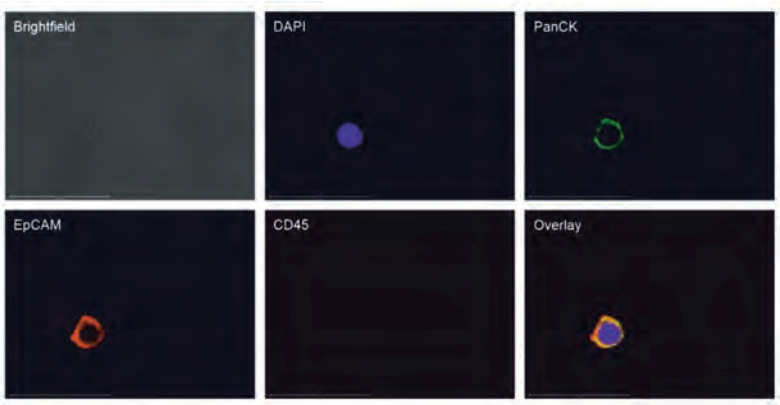
Conventional means for CTC enrichment have relied upon either immuno-affinity capture (magnetic) or size or charge-based separation (microfluidic devices). The former faces limitations with CTCs that express low amount of epitope or those which are sequestered in clusters with nonepitope expressing cells. In addition to low sensitivity, this also leads to low specificity by enriching incidental non-malignant cells that express the detection epitope. The latter has low capture rate of CTCs beyond the operational size / charge range of the device and can also enrich non-malignant cells with conform to detection parameters.

In contrast, Trucheck™ employs an epigenetically activating medium (EAM) which negatively enriches CTCs via the cancer hallmark of evading apoptosis. When isolated PBMCs are treated with the EAM, all non-malignant cells are killed by their functional apoptosis machinery, whereas all cancer derived malignant cells (CTCs) survive.



Tissue and organ of origin specific markers:

Conventional CTC based technologies infer the presence of CTC based on detection of EpCAM+, PanCK+ and CD45-cells. These technologies overlook cancers in which the cells have been shown to have other characteristics. Trucheck™ includes markers that cover various subtypes of carcinomas as well as markers specific for other cancer types (Trucheck™ intelli) such as gliomas, sarcomas and neuroendocrine tumours.



Illustrative immunochemistry images of cancer patient

Trucheck™ uses multiplexed fluorescence immunocytochemistry (ICC) to evaluated multiple markers in a single run with unique fluorophore conjugated antibodies.

Trucheck™

Sensitivity and Specificity

Clinical Validation

	Cancer vs Asymptomatic	Cancer vs Benign
Sensitivity	85.74% (85.18% - 86.29%)	85.74% (85.18% - 86.29%)
Specifictiy	99.90% (99.97% - 100%)	99.29% (98.34% - 99.77%)
Accuracy	99.97% (99.94% - 99.99%)	94.82% (94.46% - 95.15%)
PPV	99,90%	98.34% (96.11% - 99.30%)
NPV	99.97% (99.97% - 99.97%)	93.39% (93.15% - 93.63%)

Preliminary clinical validation of Trucheck™ has been performed in a blinded prospective study involving **15.441** cancers, **700** benign cases and **13.919** asymptomatic individuals to establish the clinical performance characteristics (table above).

Though Trucheck™ is not intended as a replacement for standard of care cancer screening, we benchmarked the clinical performance of Trucheck™ against standard methods. The results show that Trucheck™ is comparable to or better than established methods in terms of sensitivity and specificity, and provides an important additional contribution to diagnostics.

Trucheck™ in colon cancer detection

	Trucheck™	Colonoscopy / CT Colongraphy
Sensitivity	82.6%	73-98%[3]
Specifictiy	99.9%	89%[3,4]
PPV	99.9%	-
NPV	99.9%	-

Trucheck™ in breast cancer detection

	Trucheck™	Mammography[1]
Sensitivity	88.2%	86.9%
Specifictiy	99.9%	88.9%
PPV	99.9%	69.6%[2]
NPV	99.9%	95.9%[3,1]

Trucheck™ in prostate cancer detection

	Trucheck™	PSA[4]
Sensitivity	85.6%	90.0%
Specifictiy	99.9%	19.7%
PPV	99.9%	33.9%
NPV	99.9%	81.0%

[1] Lehman CD et al. National Performance Benchmarks for Modern Screening Digital Mammography: Update from the Breast Cancer Surveillance Consortium. Radiology. 2017 Apr; 283(1): 49-58. doi: 10.1148/radiol.2016161174.

[2] PPV and NPV Calculated from data reported by Lehman et al (above).

[3] USPSTF reported data.

[4] McKiernan J et al. A Prospective Adaptive Utility Trial to Validate Performance of a Novel Urine Exosome Gene Expression Assay to Predict High grade Prostate Cancer in Patients with Prostate - specific Antigen 2-10 ng/ml at Initial Biopsy. Eur Urol. 2018 Dec; 74(6):731-738. doi: 10.1016/j.eururo.2018.08.019.

Trucheck™

Available solutions

- Trucheck™ Breast
- Trucheck™ Prostate
- Trucheck™ Colorectal / Stomach
- Trucheck™ Diabetes (Bladder, Colorectum, Gallbladder, Kidney, Liver, Pancreas)
- Trucheck™ intelli

Publications

1. Akolkar D et al. Circulating ensembles of tumor-associated cells: A redoubtable new systemic hallmark of cancer. International Journal of Cancer. 2020; 146(12): 3485-3494. DOI: 10.1002/ijc.32815.
2. Ranade A et al. Hallmark Circulating Tumor-Associated Cell Clusters Signify 230 Times Higher One-Year Cancer Risk. Cancer Prev Res (Phila). 2020 Sep 21. doi: 10.1158/1940-6207.CAPR-20-0322. Epub ahead of print.
3. Gaya A et al. Evaluation of circulating tumor cell clusters for pan-cancer noninvasive diagnostic triaging. Cancer Cytopathol. 2021 Mar; 129(3): 226-238. doi: 10.1002/cncy.22366.

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