

Biomarker-Analytics Individualization of Cancer Diagnostics and Therapy

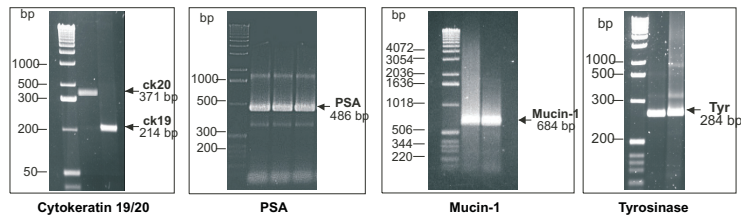
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Cancer is a disease of uncontrollable stem cells. The Dr. Kübler GmbH has a patented system available for isolation, quantification and molecular characterisation of these cells. Cancer stem cells (CSC) already circulate in the bloodstream before a primary tumour gets visible; that means revolution in prophylaxis, diagnosis and therapy. The number of CSC circulating in the bloodstream correlates with the evolution and stage of the disease. The molecular characteristics of these uncontrollable stem cells is decisive in the choice of the appropriate therapeutic agent (kinase inhibitors, monoclonal antibodies, natural killer cells, HSP proteins). The technologies of personalized medicine already exist today. ^[1-6]

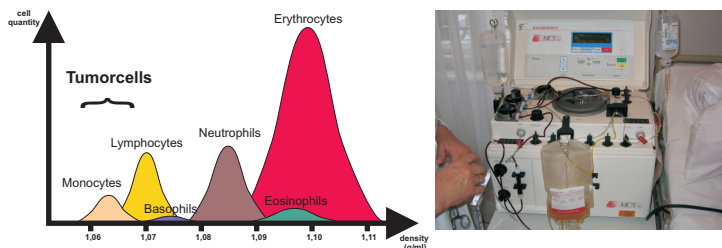
RT-PCR

The RT-PCR (reverse transcriptase-polymerase chain reaction) allows a qualitative detection of circulating epithelial cells in the bloodstream.



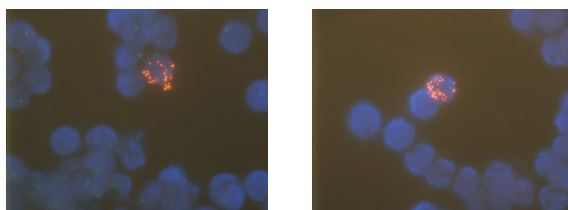
Diagnostic Apheresis

The Diagnostic Apheresis enables a quantitative extraction of circulating Cancer Stem Cells from the bloodstream and their complete molecular-pathological characterization without any biopsy. ^{[1],[4],[8]}



FISH

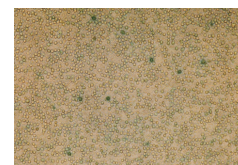
The application of FISH-Analytics (fluorescence in situ hybridisation) allows a single cell detection of cells with an amplified c-erb/B2 gene and consequently a quantification of these cells. ^[7]



c-erb/B2 gene amplification

ELISA

A specifically developed ELISA test (enzyme linked immunosorbent assay) also provides a single cell detection and consequently a quantification. Furthermore an expression profile of circulating tumor cells is created by determination of different biomarkers. ^[8]



c-Met positive cells



Oct-3/4 positive cells



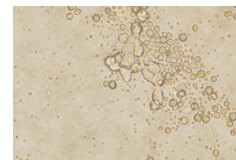
c-erb/B3 positive cell

Prognostic und predictive BIOMARKERS:

myc	CD44v5/v6
ras	VEGF
p53m	Akt/mTOR
EGFR	TKTL1
erb/B2	Indolamine deoxygenase
erb/B3	Survivin
MDR	Oct-3/4
c-Met	etc.

Therapeutic consequences

A combined immunotherapy consisting of Natural Killer cells (NK cells) and heat-shock proteins can specifically attack and destroy Cancer Stem Cells. ^[8]



NK cells



Literature

- ^[1]Dr. Kübler GmbH Deutsches Bundespatent 4228389; Europ. Patent 0.584.715; US-Patent 5,529,903; Japan. Patent JP 211352
- ^[2]Cancer Stem Cells, Jordan, CT., Guzman, ML., Noble, M., N. Engl. J. Med. 2006 355;12, 1253-61
- ^[3]Circulating Prostate Specific Antigen-positive Cells correlate with Metastatic Prostate Cancer, Hamdy FC. *et al.*, 1992 69, 392-396
- ^[4]Nachweis von Tumorstammzellen leitet Paradigmenwechsel ein Deutsches Ärzteblatt Heft 27, 07. Juli 2006
- ^[5]Tumor Cells circulate in the peripheral blood of all major carcinomas, but not in healthy subjects or patients with non-malignant diseases, Allard, J. *et al*, Clin Cancer Research 6897, 2004
- ^[6]The evidence for Cancer Stem Cells, Niederhuber, J., (NCI, Bethesda) 5th Int. H.F.C. Behr-Symposium 2008, DKFZ Heidelberg
- ^[7]Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene, Slamon, DJ., *Et al.*, Science 235, 1987, 177-182
- ^[8]Isolation and Characterization of Circulating Cancer Cells as Vaccine Candidates, Dr. Kübler GmbH, Cancer Vaccines 1996, New York
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