

Oncoproteins and circulating tumor stem cells - diagnostic and therapeutic meaning

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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]

Introduction

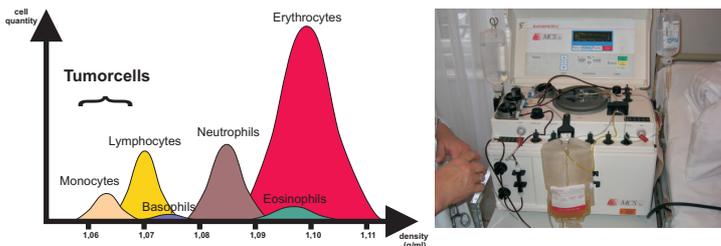
A characteristic of cancer is the appearance of circulating tumor stem cells before the primary tumor is detectable. These cells generate energy by non-oxidative degradation of glucose (Warburg's hypothesis): Akt/mTOR.

The process allows to isolate those tumor stem cells out of the blood carrying the embryonic mobility program as a result of activation of c-Met. There is a strong correlation between EMT/MET and multiple drug resistance (MDR).

The disturbance of EMT/MET is microRNA driven and correlates with metabolic changes involving the switch between oxidative phosphorylation and anaerobic glycolysis.^[9-10]

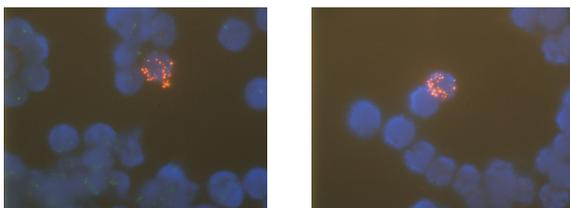
Diagnostic Apheresis

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



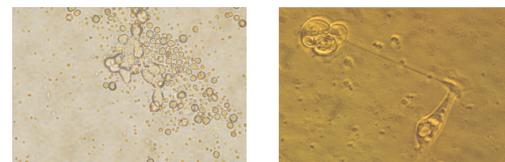
c-erb/B3 positive cell

Prognostic und predictive BIOMARKERS:

myc	CD44v5/v6
ras	VEGF
p53m	Akt/mTOR
EGFR	TKL1
erb/B2	Indolamindeoxygenase
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

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