Dr. Kübler GmbH

"CANCER IS A MOLECULAR ACCIDENT THAT OUGHT TO BE AVOIDED"

Isolation and pathway analytics of solid tumor stem cells

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Jahrestagung Deutsche Menopause Gesellschaft e.V., Frankfurt 2012

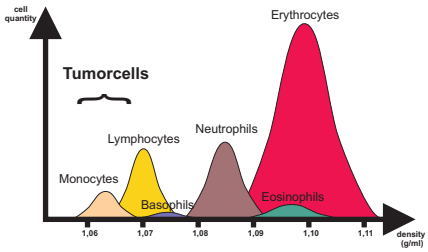
Cancer is caused by not controllable stem cells. The Dr. Kübler GmbH has a patented system available for isolation, quantification and molecular characterisation of these cells. After dissolution of epithelial cell layers Cancer Stem Cells (CSCs) can be found in the bloodstream, which have been undergone epithelio mesenchymale transition (EMT) and which represent the heterogeneity of both the primary tumor and disseminated cells. Therefore, the cells change their cell-specific characteristics and thus gain migratory capability and invasiveness. The early detection of these cells is a revolution in prevention, diagnosis and treatment. The number of CSCs circulating in the bloodstream correlates with evolution and stage of the disease. The molecular characteristics of these uncontrollable stem cells are decisive in the choice of the appropriate therapeutic agent. [1-9]

EMT (Epithelio Mesenchymale Transition)

With epithelio mesenchymale transition tumor cells gain ability for migration. The epithelio mesenchymale character of these cells is indicated by overexpression or amplification of Oct-3/4, c-met and ZEB1. If these cells have also completed the angiogenic switch (increased VEGF expression), they can recruit blood vessels, are proliferating and invasive (myc, ras, p53m, uPA). [1, 10-13]

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.[7, 16]



Proceedings

This method allows:

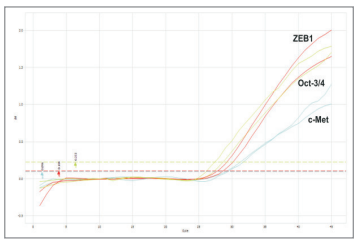
1. detection of circulating tumor stem cells without biopsy
2. quantification of these cells
3. their complete molecular characterization: c-Met, Oct-3/4, GFAP, EGFR, erb/B2, erb/B3, c-myc, ras, p53m, MDR, CD44v5/v6, VEGF, Akt/mTOR, IDO, Survivin, Urokinase

These tumor stem cells are angiogenic, they recruit their own blood vessels, they remain and proliferate in so-called stem cell niches, where they are beyond the reach of scalpel. They are resistant against chemo and radiation treatment. [1-4, 10-13]

After isolation and culturing of the tumor stem cells, we use their complete antigenic material for immunization of the patient and to initiate a NK cell response. In addition, we use biological deacetylation inhibitors and protease inhibitors, which prevent further degeneration of the tumor stem cells and protect from their invasive potential. In particular, we avoid evolutionary pressure by toxic chemotherapy and radiation therapy on the tumor stem cells. By this way, we extend the survival of patients by means of non-toxic treatment along with preservation of quality of life.

Real-Time RT-PCR

The Real-Time RT-PCR (reverse transcriptase-polymerase chain reaction) allows the detection of circulating cells with deranged epithelio-mesenchymal transition in the bloodstream.[4, 5, 11, 12, 14]



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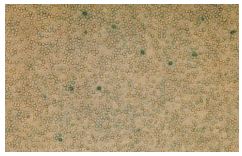
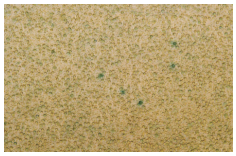
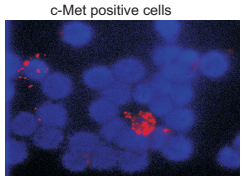
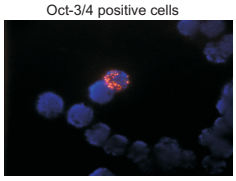
Detection

A specifically developed ELISA test (enzyme linked immuno-sorbent assay) as well as FISH techniques (fluorescence in situ hybridisation) provide a single cell detection and consequently a quantification. Furthermore an expression profile of circulating tumor cells is created by determination of different biomarkers.[7, 15]


c-Met positive cells

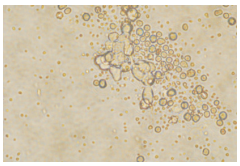

Oct-3/4 positive cells


MET gene amplifikation


c-erb/B2 gene amplifikation

Therapeutic consequences

A combined immunotherapy consisting of Natural Killercells (NK cells) and heat-shock proteines can specifically attack and destroy Cancer Stem Cells.[7]


NK cells

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Further Literature: www.kueblergmbh.com