LABOR – PRAXISKLINIK GbR
DR. KÜBLER & PARTNER

Cellular diagnostics and molecular therapy of diseases and function disorders of the brain

Dr. U. Kübler, J. Kübler, Dr. J. Schnepel

Brain Tumor 2015, Berlin

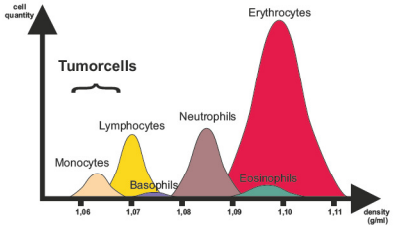
Glial cells perform many functions in the Central Nervous System (CNS), e.g. providing structural support and defining brain architecture. They are also indispensable for neurogenesis and development of the CNS. Diagnostic gliapheresis (EP1486787B1) is a patented cell collecting system, which enables the isolation, quantification and molecular characterization of circulating glial cells emitted from the brain into the bloodstream. This is not only possible with malignancies but also with multisystem atrophies, Alzheimer's disease and not yet understood glial disorders. With this method the pathophysiology of glial disorders can be examined for the first time *in vitro* without biopsy. Thus target-specific, diagnostic and therapeutic consequences became possible.[1,2]

Introduction

Glial cells are the immune cells of the central nervous system (CNS). They communicate as sensors with the neurons and the environment and respond to endogenous and exogenous transcription factors, for example, PDGF from platelets.
Using diagnostic apheresis (= Gliapheresis), the influence of different substances and other drugs on the number and the molecular expression profile of circulating glial cells can be examined.
In this way, diseases and disorders of the brain can be decrypted and the response on therapies can be studied without side effects in patients.[1-4]

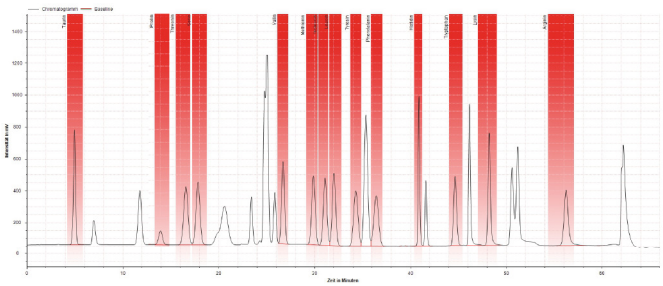
Gliapheresis

Diagnostic Apheresis enables a quantitative extraction of GFAP expressing cells from the bloodstream and their complete molecular-pathological characterization without biopsy. In addition biomarkers like c-Met, Oct-3/4, GFAP, EGFR, erb/B2, erb/B3, myc, ras, p53m, MDR, CD44v5/v6, VEGF, Akt/mTOR, IDO, Survivin, or Urokinase can provide information about metastasis initiating Cancer Stem Cells (MICs).[2]



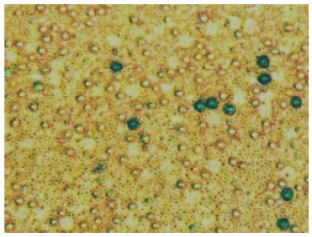
GFAP und amino acids

Neurotransmitters and intermediate filaments such as GFAP are made of essential amino acids by the glial cells. In case of malfunctions of the immune system, such as attacks of aggressive lymphocytes on glial cells, there is a disturbance of the dialogue between glial cells and neurons. This has effects on the dopaminergic, serotonergic, gabaminergic and glutaminergic system of neuronal and glial transmitters, e.g. in connection with burnout-syndrome. Typical symptomes in such cases are deficiancies of neurotropic amino acids such as lysine or proline.[5]

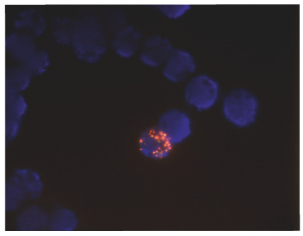


Detection

A specifically developed ELISA test (enzyme-linked immunosorbent 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 cells is created by determination of different biomarkers.[2]



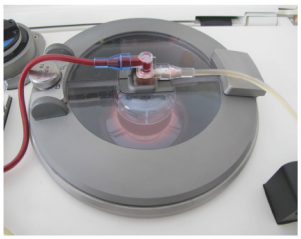
GFAP positive Cells



MET gene amplification

Therapeutic consequences

Affecting of GAFP synthesis by substitution of amino acids lysine and proline and by administration of GDF (growth differentiation factor), which can be isolated from apheretic obtained autologous platelets homologously.[3,4,6,7]



Literature

[1]Glial Physiology and Pathophysiology, Verkhratsky, A. and Butt, A., 2013, Wiley-Blackwell, 4.6 Functions of Astroglia, 175-179.
[2]Process for the *in vitro* diagnosis of a glioma or an astrocytoma and a pharmaceutical mixture for the treatment, Kübler, U., 2011, Eur. Patent EP1486787B1.
[3]Vascular and neurogenic rejuvenation of the aging mouse brain by young systemic factors, Katsimpardi, L. *et al.*, Science 2014, 344 (6184), 630-634.
[4]Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice, Villeda, S. A. *et al*, Nature Medicine 2014, 20 (6), 659-663.
[5]Genetic disorders affecting astocytes, Messing, A. and Brenner, M. in Neuroglia, Third Edition by Kettenmann, H. and Ransom B.R., 2013, 884-895.
[6]Gap junctions and hemichannels, Ransom, B.R. and Giaume, C. in Neuroglia, Third Edition by Kettenmann, H. and Ransom B.R., 2013, 292-305.
[7]Astroglial networks: a step further in neuroglial and gliovascular interactions, Giaume, C. *et al*, Nat. Rev. Neuroscience 2010, 11, 87-99.

Labor-Praxisklinik GbR
Dr. Kübler & Partner
Siebertstr. 6
81675 München
www.labor-praxisklinik.de
info@labor-praxisklinik.de