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## Marburg cerebrospinal fluid (CSF) model reveals CSF constituents as new CSF biomarkers

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In healthy humans CSF (total: ≈150 ml) flows from ventricles V1-V4 into subarachnoid/spinal spaces, where CSF is absorbed. CSF cellular and protein constituents are controlled by blood-CSF barrier (bCSFb) in 4 choroid plexus (main CSF production) and blood-brain barrier (bbb) in brain capillaries, sealed with tight-tight junctions. Cellular constituents are leukocytes (mainly lymphocytes): 0-1/μl in ventricle V-CSF, 1-3/μl in cistern C-CSF, 1-5/μl in lumbar L-CSF; representing 2 cellular biomarkers: 'V/C-CSF leukocytes' evaluate penetration of blood leukocytes pressed through circum-ventricular organs (without bbb) into V-CSF by blood pressure; - 'L-CSF lymphocytes' uncover reflux rate of lymph lymphocytes when lumbar CSF drains out into thoracic duct. L-CSF leukocytes are sum of C-CSF blood leukocytes + L-CSF lymph leukocytes. CSF protein levels are dependent on their molecular weight: albumin >IgG >IgA >IgM and reveal filtration of blood proteins into V-CSF through bCSFb less-tight junctions and basal membrane (no barrier with plexus capillaries/venules). Biomarkers 'CSF proteins' reveal a) penetration capacity of blood proteins through bCSFb into V CSF, b) flow rate of V-CSF into L-CSF, c) concentration of CSF draining along cranial and spinal nerves: small proteins (albumin) drain out easier than large ones (IgM); thus summarizing the CSF sink effect. Summary: The new biomarkers renew CSF patho-biochemistry, thus improving human CSF diagnostics, revealed with Marburg CSF Model.

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## Exosomes as a signature for the progress and metastatic potential of pancreatic cancer

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Pancreatic cancer is the fourth most common cause of death due to cancer in the world. Pancreatic cancer is known to have a poor prognosis, mostly due to the fact that early stages of the disease are generally asymptomatic. Progress in pancreatic cancer research has been slow, leaving several fundamental questions pertaining to diagnosis and treatment unanswered. Recent studies highlight the putative utility of tissue-specific vesicles (i.e extracellular vesicles) in the diagnosis of disease onset and treatment monitoring in pancreatic cancer. Extracellular vesicles (EVs) are membrane limited structures derived from the cell membrane. They contain specific molecules including proteins, mRNA, microRNAs and non-coding RNAs that are secreted to the extracellular space. EVs can be classified according their size and/or origin into microvesicles (~150-1000 nm) and exosomes (~40-120 nm). Microvesicles are released by budding from the plasmatic membrane, whereas exosome release is by fusion of multivesicular bodies with the plasmatic membrane. In this review, we discuss our current knowledge in the diagnosis and treatment of pancreatic cancer and the potential role of EVs with a special emphasis in exosomes. We suggest that as exosomes contain cellular protein and RNA molecules in cell type-specific manner, they may provide extensive information about the signature of the tumour and pancreatic cancer progression. To date, our research will be the first to analyse the potential of exosomes from pancreatic cyst fluid as a biomarker for the early detection of pancreatic cancer.

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