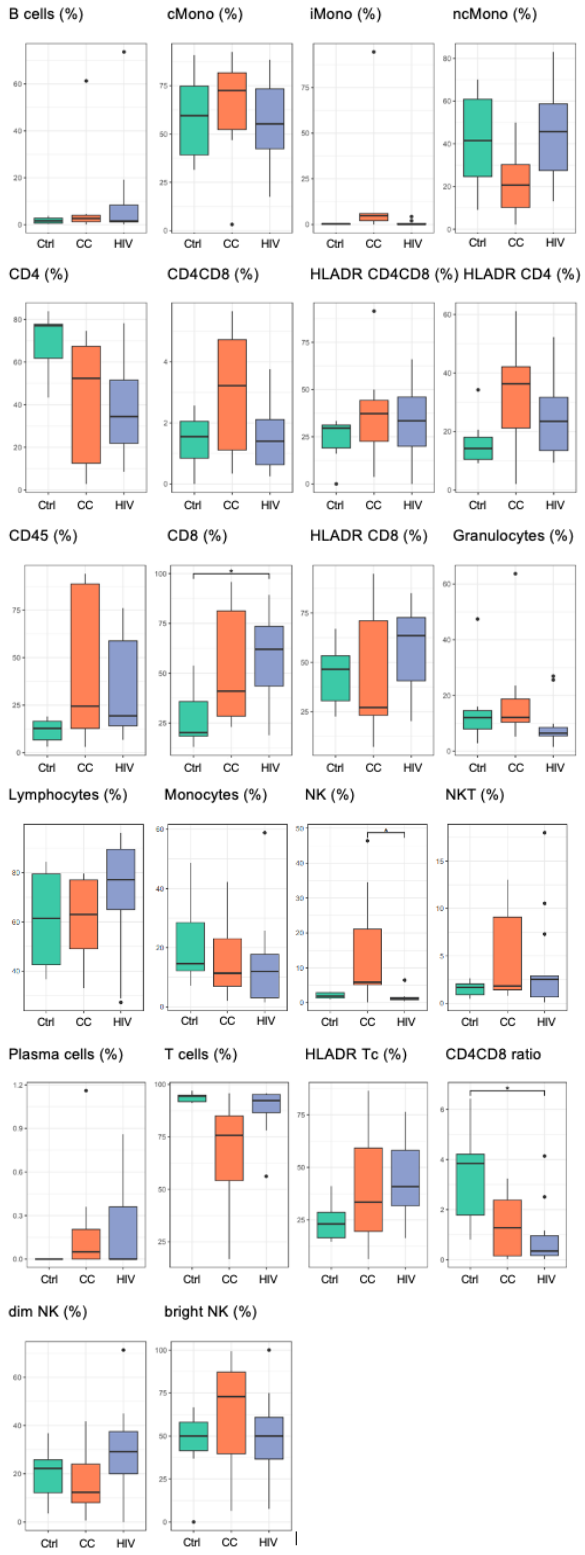
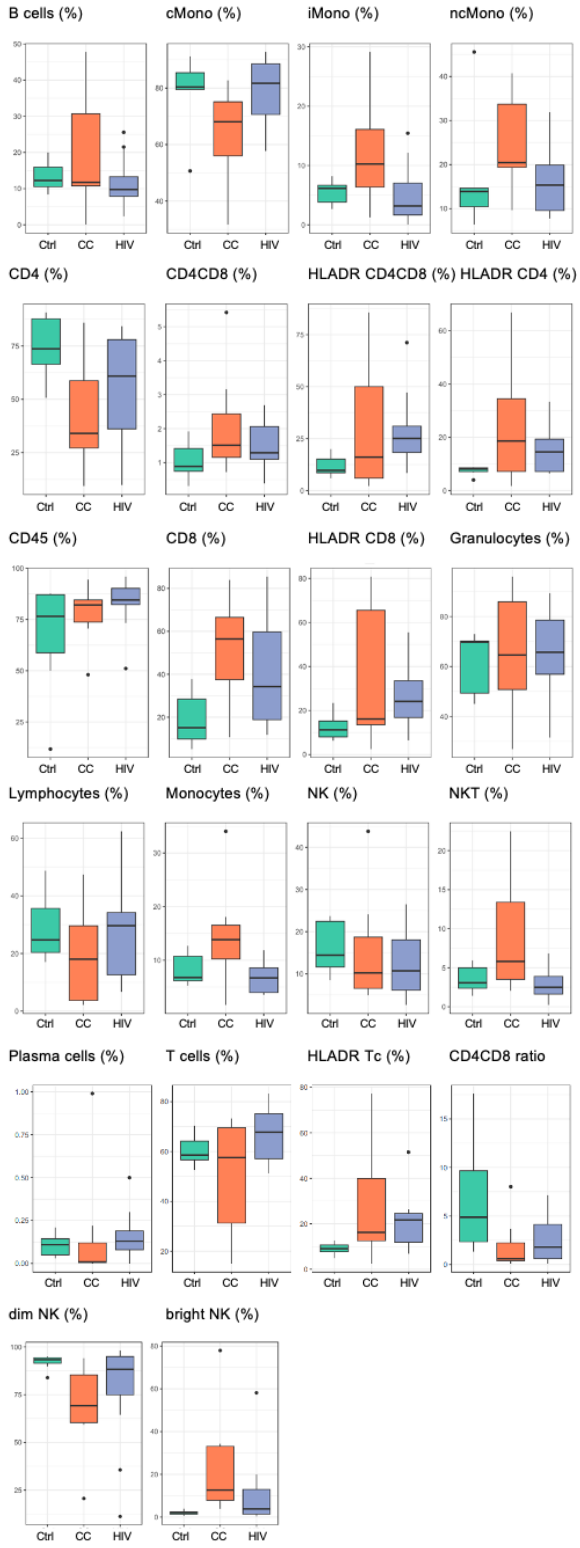
Supplementary Figure 1: Comparison of cellular subpopulations in the CSF of CC and control groups



Supplementary Figure 1: Plotting of individual mFc parameters revealed a significant increase of NK cells in the CSF of the CC group. Other cellular subpopulations showed no alteration in the CSF of CC patients compared to HIV and Ctrl.

Abbreviations - Bc: B lymphocytes, bright NK: $CD56^{bright}$ natural killer cells, CC: cryptococcal meningitis, CD45: leukocytes, cMono: classical monocytes, CSF: cerebrospinal fluid, Ctrl: healthy control group, dim NK: $CD56^{dim}$ natural killer cells, Granulo: granulocytes, HIV: *human immunodeficiency virus* positive, immunocompromised control group, HLA-DR Tc: activated T cells, Lympho: lymphocytes, iMono: intermediate monocytes, mFC: multicolor flow cytometry data, mono: monocytes, ncMono: non-classical monocytes, NK: natural killer cells, NKT: natural killer T cells, Plasma: plasma cells, Tc: T lymphocytes

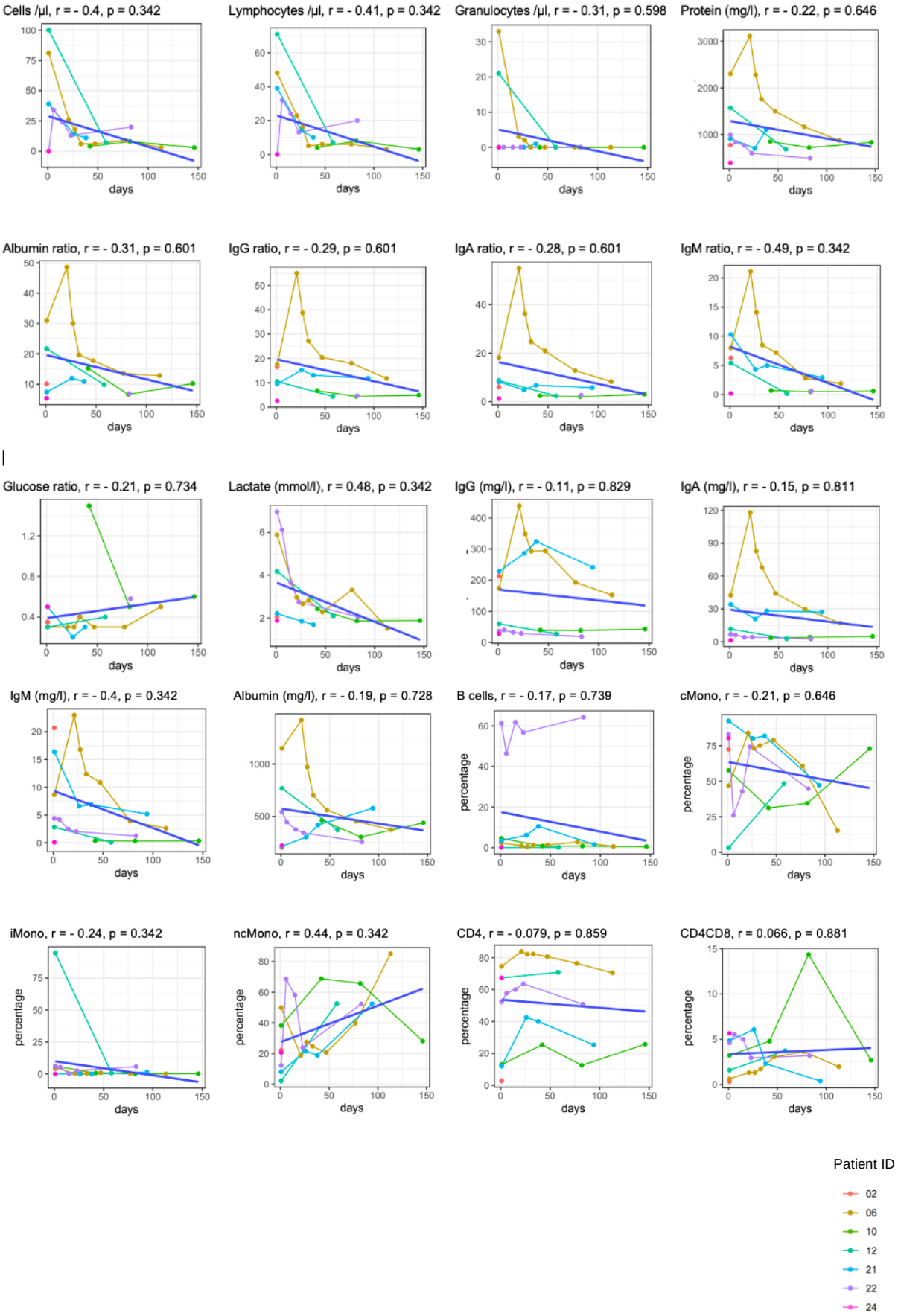
Supplementary Figure 2: Comparison of cellular subpopulations in the blood of CC and control groups

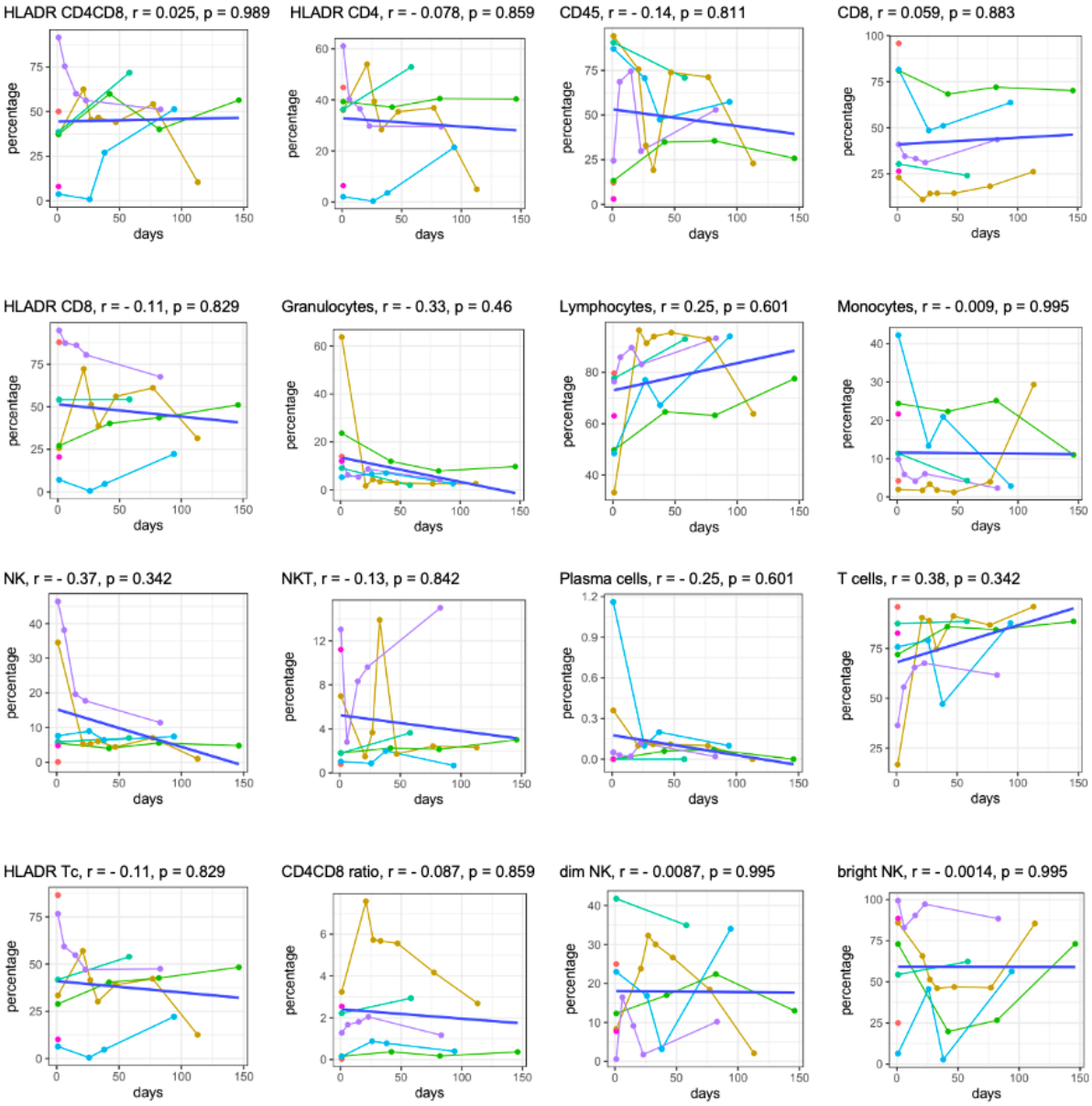


Supplementary Figure 2: Plotting of individual mFc parameters revealed an increase of CD56^{bright} natural killer cells in blood of CC patients compared to the HIV and Ctrl group.

Abbreviations - Bc: B lymphocytes, brightNK: CD56^{bright} natural killer cells, CC: cryptococcal meningitis, CD45: leukocytes, cMono: classical monocytes, CSF: cerebrospinal fluid, Ctrl: healthy control group, dimNK: CD56^{dim} natural killer cells, Granulo: granulocytes, HIV: *human immunodeficiency virus* positive, immunocompromised control group, HLA-DR Tc: activated T cells, Lympho: lymphocytes, iMono: intermediate monocytes, mFC: multicolor flow cytometry data, mono: monocytes, ncMono: non-classical monocytes, NK: natural killer cells, NKT: natural killer T cells, Plasma: plasma cells, Tc: T lymphocytes

Supplementary Figure 3: Reconstitution kinetics of cellular subsets in the CSF under antifungal therapy

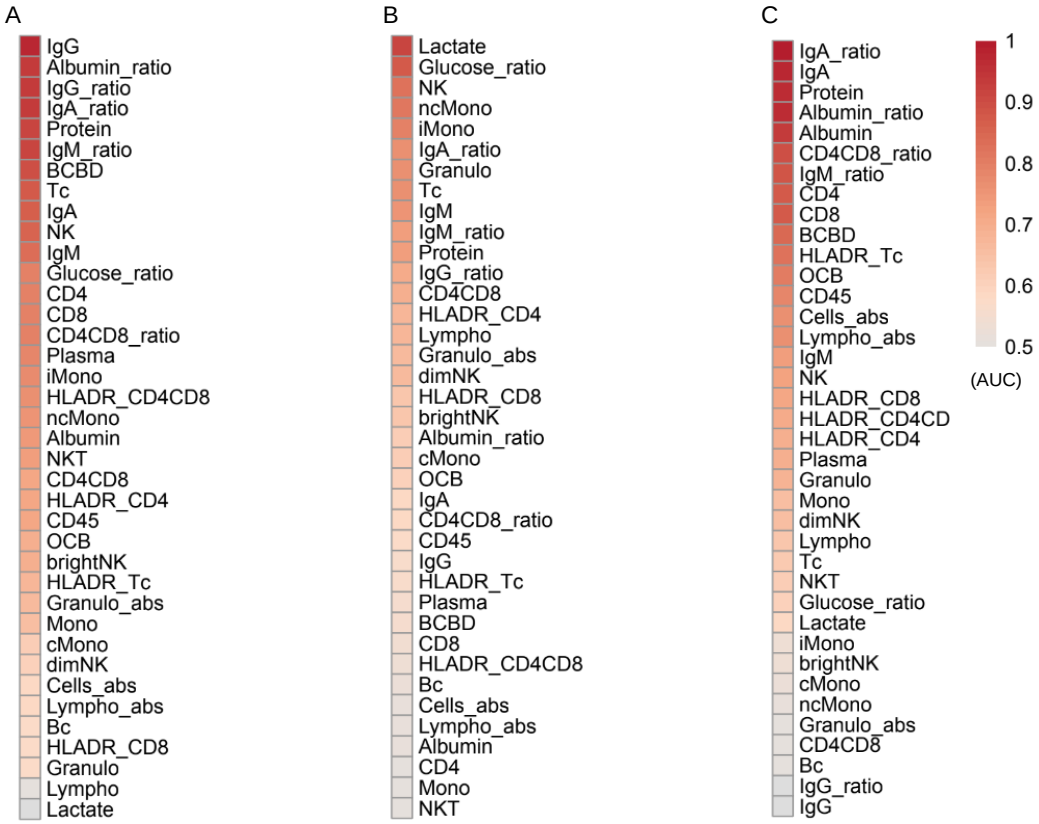




Supplementary Figure 3: Reconstitution kinetics of CSF parameters. Slow normalization of standard CSF parameters in CC patients under antifungal therapy. Parameters of each patient are presented as individual lines of the same color. Flow cytometry of CSF was performed at the first presentation of each patient and during follow-up in different intervals. Antifungal therapy was started within days after the first diagnosis of cryptococcal meningitis. Samples were taken in different time intervals, trends of each parameter are represented over a period of 150 days. First sample (day 0) of patient 10 and patient 24 were taken during follow up, both were already on antifungal therapy (Patient 10: 10 months after first diagnosis; Patient 24: 30 months after first diagnosis). Correlation analysis was performed with Pearson's correlation coefficient and p values were adjusted with the Benjamini-Hochberg method.

Abbreviations – abs: absolute cell counts, Bc: B lymphocytes, BCBD: blood-CSF-barrier disruption, brightNK: $CD56^{bright}$ natural killer cells, CC: cryptococcal meningitis, cMono: classical monocytes, CSF: cerebrospinal fluid, Ctrl: healthy control group, dimNK: $CD56^{dim}$ natural killer cells, Granulo: granulocytes, HIV: *human immunodeficiency virus* positive, immunocompromised control group, HLA-DR Tc: activated T cells, IgA: immunoglobulin A, IgG: immunoglobulin G, IgM: immunoglobulin M, iMono: intermediate monocytes, Lympho: lymphocytes, Mono: monocytes, ncMono: non-classical monocytes, NK: natural killer cells, NKT: natural killer T cells, Plasma: plasma cells, Tc: T lymphocytes

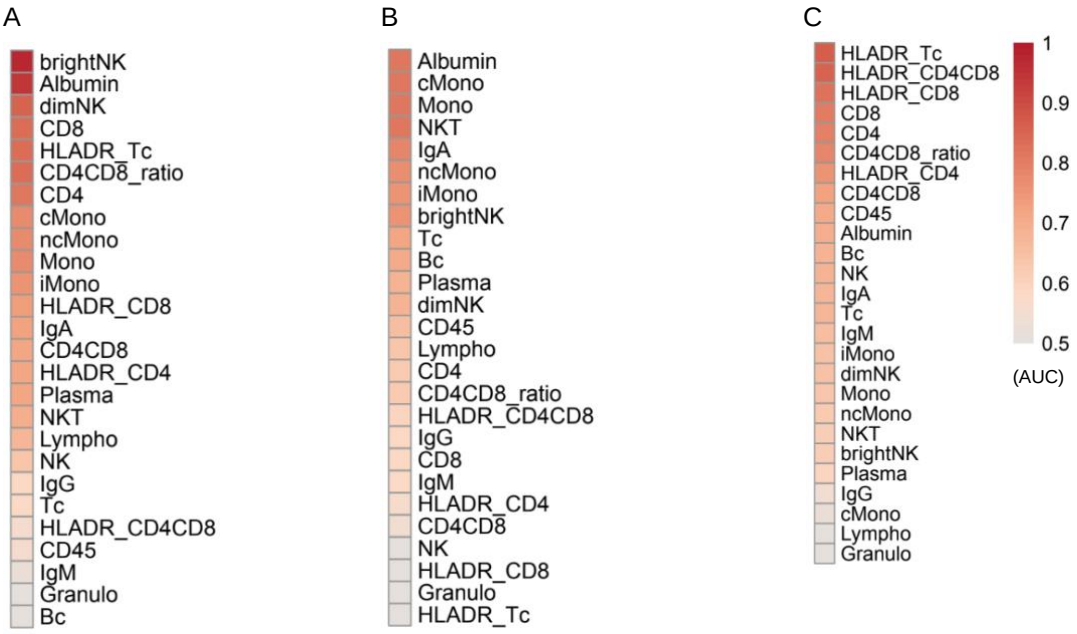
Supplementary Figure 4: ROC analysis of CSF parameters



Supplementary Figure 4: Receiver operating characteristic (ROC) analysis of CSF parameters. Sensitivity and specificity are represented by area under the curve (AUC) values, which range from 1 (perfect distinction) to 0.5 (uninformative). Heatmaps illustrate the hierarchy of all parameters according to their distinctive power when comparing (A) CC vs. Ctrl (B) CC vs. HIV and (C) HIV vs. Ctrl. AUC values are listed in Supplementary Table 3.

Abbreviations – abs: absolute cell counts, Bc: B lymphocytes, BCBD: blood-CSF-barrier disruption, brightNK: $CD56^{bright}$ natural killer cells, CC: cryptococcal meningitis, cMono: classical monocytes, CD45: leukocytes, CSF: cerebrospinal fluid, Ctrl: healthy control group, dimNK: $CD56^{dim}$ natural killer cells, Granulo: granulocytes, HIV: *human immunodeficiency virus* positive, immunocompromised control group, HLA-DR Tc: activated T cells, IgA: immunoglobulin A, IgG: immunoglobulin G, IgM: immunoglobulin M, iMono: intermediate monocytes, Lympho: lymphocytes, mFC: multicolor flow cytometry data, Mono: monocytes, ncMono: non-classical monocytes, NK: natural killer cells, NKT: natural killer T cells, OCB: oligoclonal bands, Plasma: plasma cells, Tc: T lymphocytes

Supplementary Figure 5: ROC analysis of blood parameters



Supplementary Figure 5: Receiver operating characteristic (ROC) analysis of blood parameters. Sensitivity and specificity are represented by area under the curve (AUC) values, which range from 1 (perfect distinction) to 0.5 (uninformative). Heatmaps illustrate the hierarchy of all parameters according to their distinctive power when comparing (A) CC vs. Ctrl (B) CC vs. HIV and (C) HIV vs. Ctrl. AUC values are listed in Supplementary Table 3.

Abbreviations – abs: absolute cell counts, Bc: B lymphocytes, BCBD: blood-CSF-barrier disruption, brightNK: $CD56^{bright}$ natural killer cells, CC: cryptococcal meningitis, cMono: classical monocytes, CD45: leukocytes, CSF: cerebrospinal fluid, Ctrl: healthy control group, dimNK: $CD56^{dim}$ natural killer cells, Granulo: granulocytes, HIV: *human immunodeficiency virus* positive, immunocompromised control group, HLA-DR Tc: activated T cells, IgA: immunoglobulin A, IgG: immunoglobulin G, IgM: immunoglobulin M, iMono: intermediate monocytes, Lympho: lymphocytes, mFC: multicolor flow cytometry data, Mono: monocytes, ncMono: non-classical monocytes, NK: natural killer cells, NKT: natural killer T cells, OCB: oligoclonal bands, Plasma: plasma cells, Tc: T lymphocytes