# Supplemental information

# Physical phenotype of blood cells is altered in COVID-19

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1                                 **Supplementary Figures and Tables**

**Supplementary table 1.** Patient characteristics, medical management and outcome of all donors included in this study.

| | All donors n=54 (100%) | | |
| --- | --- | --- | --- |
| | **Control n=24** | **Recovered n=14** | **COVID-19 n=17** |
| **Age (years): median (range)** | 62.5 ± 13.6 years (26-81) | 58.6 ± 12.4 (27-76) | 68·± 10.4 (41-87) |
| **Gender** | | | |
| male | 12 (50%) | 10 (71.4%) | 13 (76.5%) |
| female | 12 (50%) | 4 (18.6%) | 4 (23.5%) |
| **Primary virus identification (PCR airway)** | n.a. | 14 (100%) | 17 (100%) |
| **Complications and medical management** | | | |
| Oxygen supplementation | 0 | 0 | 17 (100%) |
| Mechanical ventilation | 0 | 0 | 13 (76.5%) |
| ECMO | 0 | 0 | 6 (35.3%) |
| Dialysis | 0 | 0 | 3 (17.6%) |
| Systemic Superinfection | 0 | 0 | 7 (41.1%) |
| Pulmonary embolism | 0 | 0 | 6 (35.3%) |
| **Drugs** | | | |
| Azithromycin | 0 | 0 | 3 (17.6%) |
| Hydroxychloroquine | 0 | 0 | 9 (52.9%) |
| Heparin prophylactic/therapeutic anticoagulation | 0 | 0 | 13 (76.5%) |
| **Outcome** | | | |
| Length of hospital stay (days) | 0 | 7 ± 2.4 (5-12) | 22.8 ± 14 (7-50) |
| Intensive care unit stay | 0 | 0 | 13 (76.5%) |
| Discharged | 0 | 14 (100%) | 9 (52.9%) |
| Further hospitalized | 0 | 0 | 0 |
| Death | 0 | 0 | 8 (47.1%) |

2  **Supplementary table 2.** Kruskal-Wallis *H*-statistics, *p*-values and effect sizes ε². The last three columns
3  represent *p*-values from Dunn's posthoc tests conducted for the significant results of Kruskal-Wallis *H*-
4  tests.

| A - healthy<br>B- recovered<br>C - COVID | *p* (Kruskal-Wallis) | *H* (Kruskal-Wallis) | $\varepsilon^2$ (Kruskal-Wallis) | *p* AC (Dunn's) | *p* AB (Dunn's) | *p* BC (Dunn's) |
|---|---|---|---|---|---|---|
| **Erythrocytes** | | | | | | |
| **Median area** | 0.1162 | 4.30 | 0.080 | 0.4896 | 0.1503 | 1.0000 |
| **SD area** | 0.0000 | 26.99 | 0.500 | 0.0000 | 0.2259 | 0.0112 |
| **Median volume** | 0.2532 | 2.75 | 0.051 | 1.0000 | 0.2938 | 1.0000 |
| **SD volume** | 0.0000 | 33.75 | 0.625 | 0.0000 | 0.9204 | 0.0002 |
| **Median deformation** | 0.2180 | 3.05 | 0.056 | 0.4480 | 1.0000 | 0.3380 |
| **SD deformation** | 0.0000 | 42.30 | 0.783 | 0.0000 | 0.0024 | 0.0340 |
| **% of ery with def < 0.28** | 0.0000 | 25.83 | 0.478 | 0.0000 | 1.0000 | 0.0016 |
| | | | | | | |
| **Neutrophils** | | | | | | |
| **Median area** | 0.0000 | 22.95 | 0.425 | 0.0000 | 0.2704 | 0.0260 |
| **SD area** | 0.0001 | 18.86 | 0.349 | 0.0023 | 0.0001 | 0.6791 |
| **Median volume** | 0.0000 | 23.53 | 0.436 | 0.0000 | 0.1319 | 0.0517 |
| **SD volume** | 0.0001 | 19.78 | 0.366 | 0.0005 | 0.0002 | 1.0000 |
| **Median deformation** | 0.0013 | 13.31 | 0.246 | 0.0021 | 1.0000 | 0.0319 |
| **SD deformation** | 0.0059 | 10.28 | 0.190 | 0.0041 | 0.3772 | 0.5059 |
| **Median Young's modulus** | 0.1698 | 3.55 | 0.066 | 0.1827 | 1.0000 | 0.8807 |
| | | | | | | |
| **Lymphocytes** | | | | | | |
| **Median area** | 0.0499 | 6.00 | 0.111 | 0.1667 | 1.0000 | 0.0939 |
| **SD area** | 0.0000 | 30.78 | 0.570 | 0.2270 | 0.0010 | 0.0000 |
| **Median volume** | 0.0814 | 5.02 | 0.093 | 0.3403 | 1.0000 | 0.1134 |
| **SD volume** | 0.0000 | 28.36 | 0.525 | 0.7403 | 0.0003 | 0.0000 |
| **Median deformation** | 0.0132 | 8.66 | 0.160 | 0.0107 | 0.1945 | 1.0000 |
| **SD deformation** | 0.0000 | 35.61 | 0.659 | 0.0043 | 0.0218 | 0.0000 |
| **Median Young's modulus** | 0.0029 | 11.68 | 0.216 | 0.0029 | 0.0542 | 1.0000 |
| | | | | | | |
| **Monocytes** | | | | | | |
| **Median area** | 0.0000 | 30.64 | 0.567 | 0.0000 | 0.0001 | 1.0000 |
| **SD area** | 0.0011 | 13.65 | 0.253 | 0.0007 | 0.0892 | 0.7682 |
| **Median volume** | 0.0000 | 27.71 | 0.513 | 0.0000 | 0.0001 | 1.0000 |
| **SD volume** | 0.0001 | 18.48 | 0.342 | 0.0001 | 0.0075 | 1.0000 |
| **Median deformation** | 0.7918 | 0.47 | 0.009 | 1.0000 | 1.0000 | 1.0000 |
| **SD deformation** | 0.4949 | 1.41 | 0.026 | 0.7256 | 1.0000 | 1.0000 |
| **Median Young's modulus** | 0.7763 | 0.51 | 0.009 | 1.0000 | 1.0000 | 1.0000 |
| | | | | | | |
| **Eosinophils** | | | | | | |
| **Median area** | 0.1289 | 4.10 | 0.076 | 0.6099 | 0.1547 | 1.0000 |
| **SD area** | 0.0126 | 8.7600 | 0.162 | 0.1245 | 0.0168 | 1.0000 |
| **Median volume** | 0.2532 | 2.75 | 0.051 | 1.0000 | 0.2938 | 1.0000 |
| **SD volume** | 0.0000 | 33.75 | 0.625 | 0.0000 | 0.9204 | 0.0002 |
| **Median deformation** | 0.4143 | 1.76 | 0.033 | 1.0000 | 0.9095 | 0.5981 |
| **SD deformation** | 0.5965 | 1.03 | 0.019 | 1.0000 | 1.0000 | 0.9290 |
| **Median Young's modulus** | 0.9592 | 0.08 | 0.002 | 1.0000 | 1.0000 | 1.0000 |
| | | | | | | |
| **% of WBC** | | | | | | |
| **% neutrophils** | 0.0105 | 9.10 | 0.169 | 0.0499 | 1.0000 | 0.0174 |
| **% lymphocytes** | 0.0007 | 14.63 | 0.271 | 0.0006 | 0.2426 | 0.0328 |
| **% monocytes** | 0.0151 | 8.38 | 0.155 | 0.0244 | 1.0000 | 0.0644 |
| **% eosinophils** | 0.0010 | 13.73 | 0.254 | 0.1576 | 0.0007 | 0.1970 |
| **NLR** | 0.0022 | 12.22 | 0.226 | 0.0031 | 0.7018 | 0.0252 |
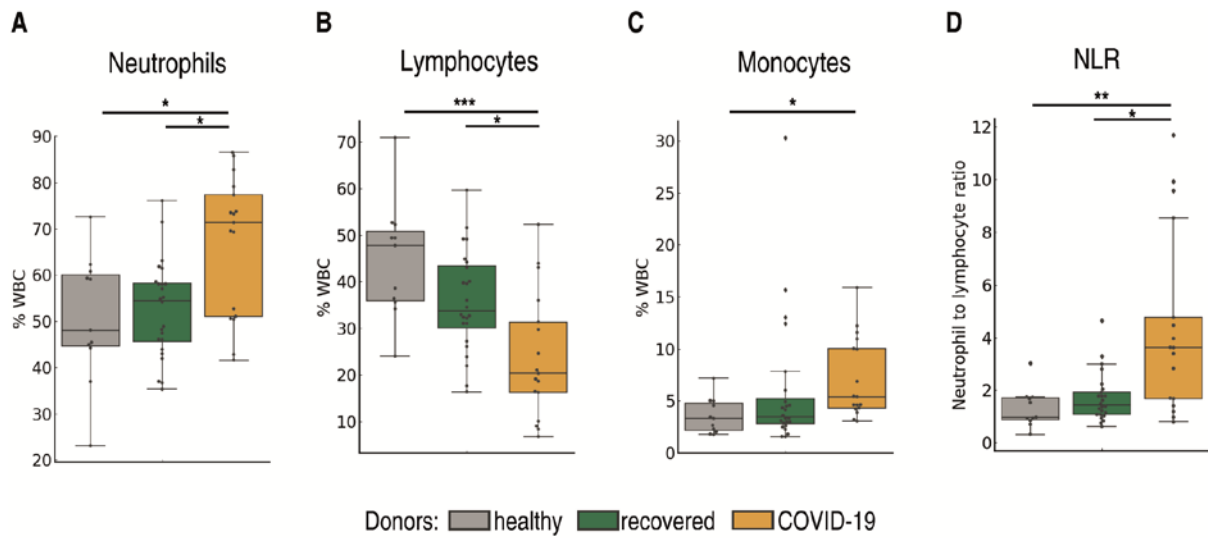
**Supplementary figure 1. Proportions of white blood cells calculated from real-time deformability cytometry (RT-DC) data.** The percentage of A) neutrophils, B) lymphocytes and C) monocytes in the total white blood cell count; a comparison of the control blood donor cohort (grey), recovered patients (green) and hospitalized COVID-19 patients (yellow). D) The neutrophil to lymphocyte ratio is significantly higher in hospitalized patients compared to the recovered and healthy donor cohorts, * $p$ < .05, ** $p$ < .01, *** $p$ < .001.
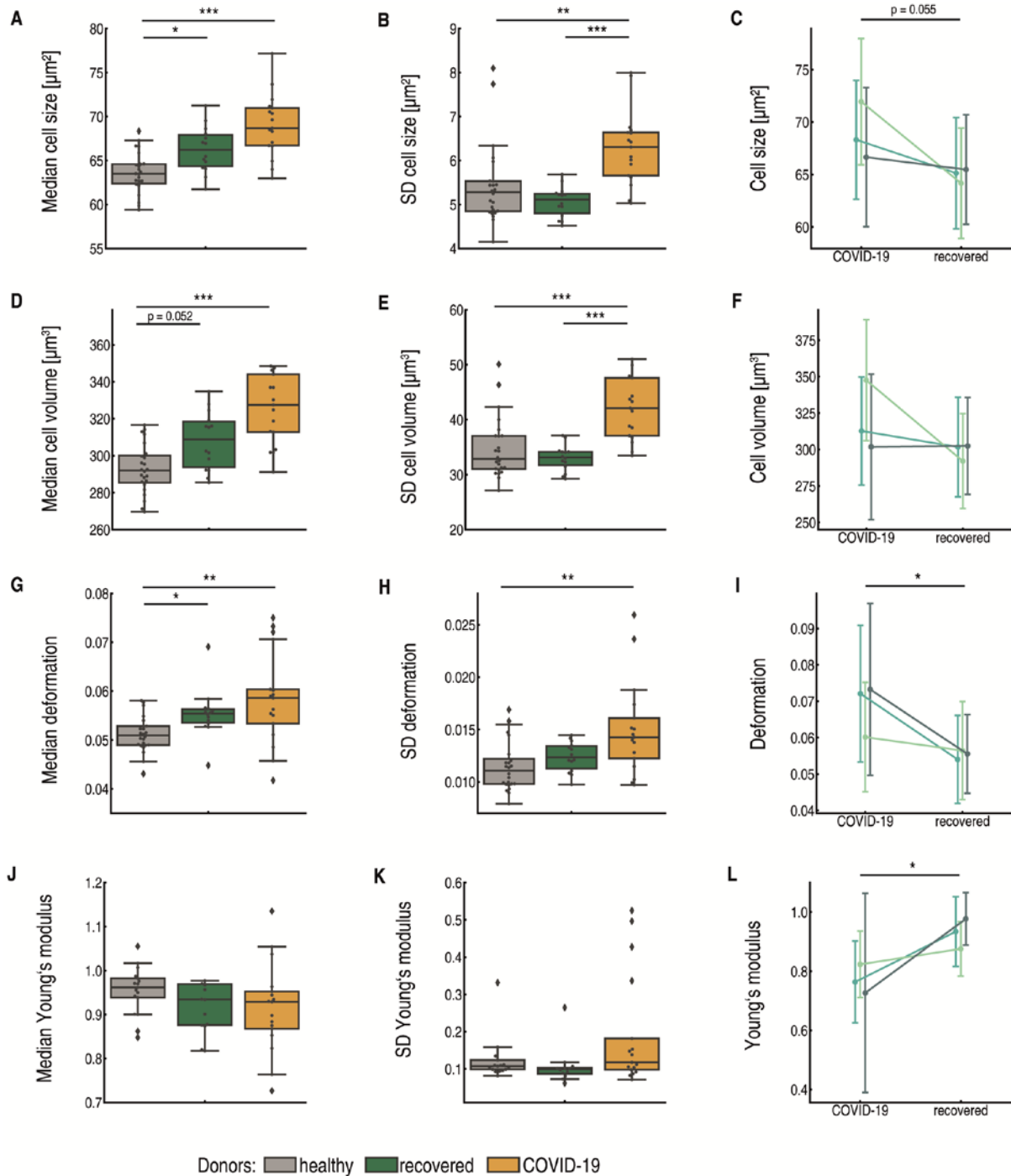
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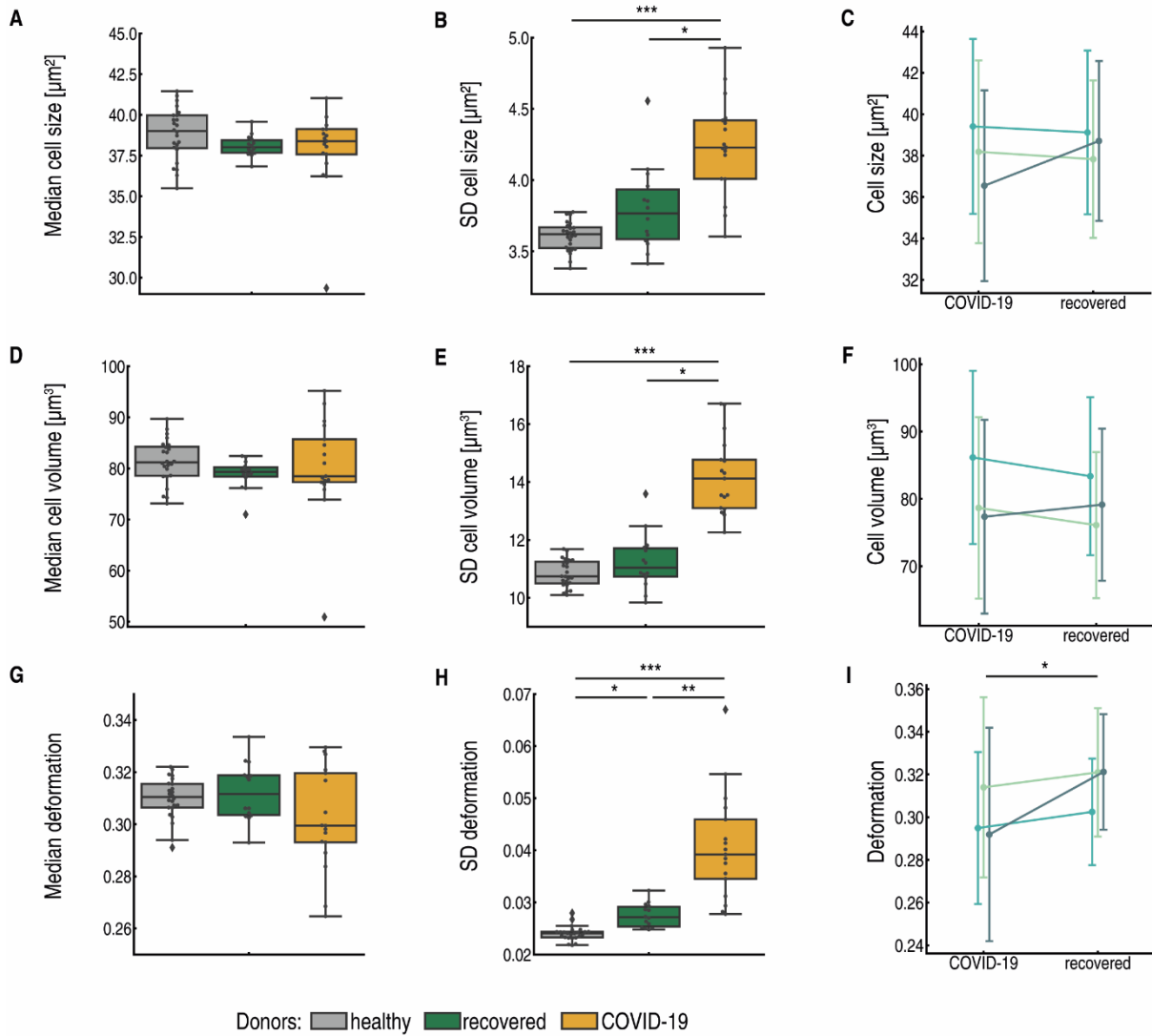
**Supplementary figure 2. Physical properties of erythrocytes of COVID-19 patients compared to controls.** Quantification of A-C) cross-sectional cell area, D-F) cell volume, G-I) cell deformation; in these graphs COVID-19 patients (yellow, n = 17) are compared to recovered donors (green, n = 14) and healthy donors (grey, n = 24). Panels C), F), I) show three patients measured at two time points, during COVID-19 and after recovery; circle markers represent the median value and error bars represent the standard deviation for each patient. Statistical comparisons in C), F), I) were performed using linear mixed model analysis. All other statistical comparisons were done using Kruskal-Wallis test with Dunn's posthoc test. * $p < .05$, ** $p < .01$, *** $p < .001$.

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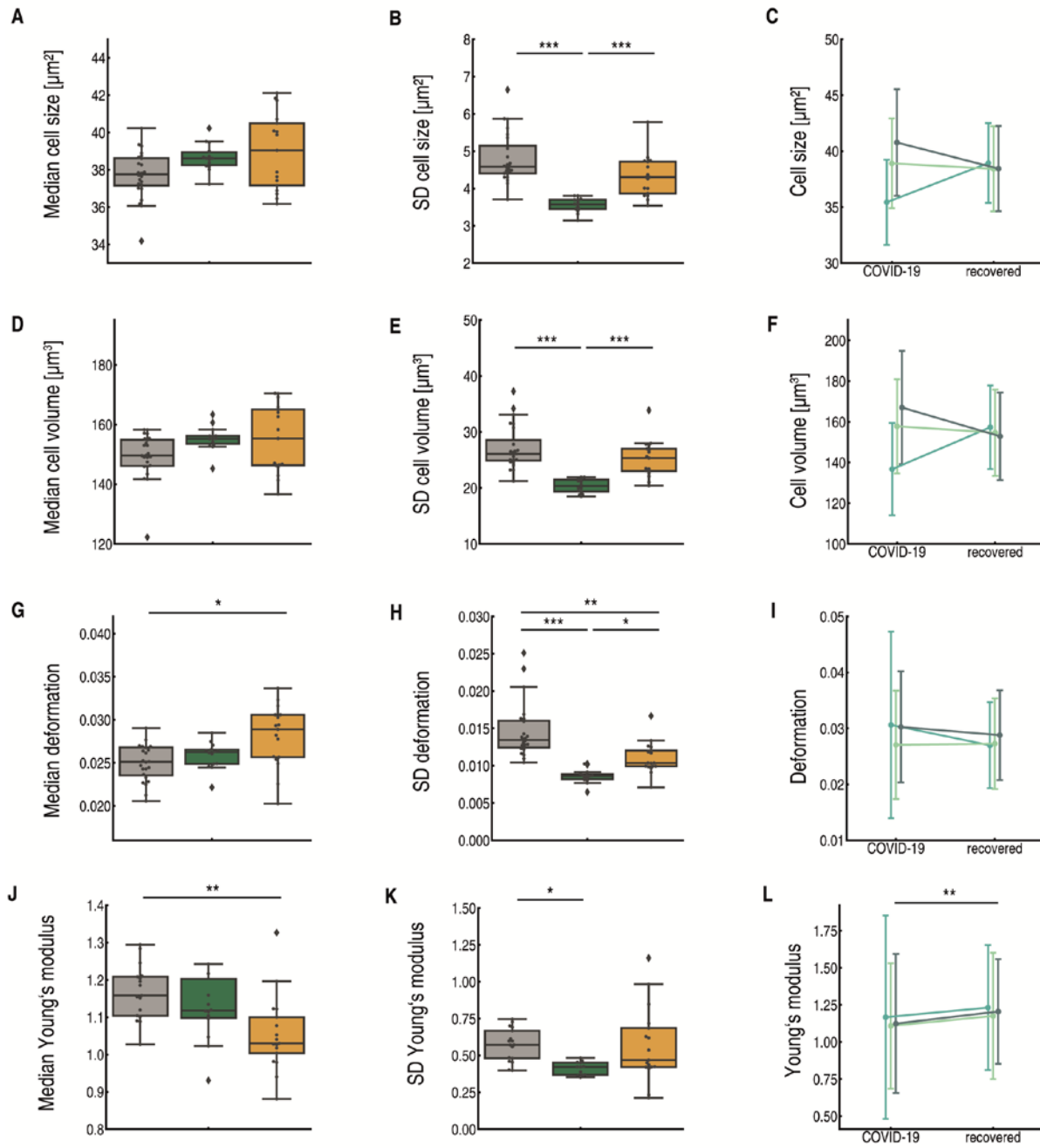
**Supplementary figure 3. Physical properties of lymphocytes of COVID-19 patients compared to controls.** Quantification of A-C) cross-sectional cell area, D-F) cell volume, G-I) cell deformation, J-L) Young's modulus; in these graphs COVID-19 patients (yellow, n = 17) are compared to recovered donors (green, n = 14) and healthy donors (grey, n = 24). Panels C), F), I) and L) show three patients measured at two time points, during COVID-19 and after recovery; circle markers represent the median value and error bars represent the standard deviation for each patient. Statistical comparisons in C), F), I), L) were performed using linear mixed model analysis. All other statistical comparisons were done using Kruskal-Wallis test with Dunn's posthoc test. * $p < .05$, ** $p < .01$, *** $p < .001$.

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**Supplementary figure 4. Physical properties of monocytes of COVID-19 patients compared to controls.** Quantification of A-C) cross-sectional cell area, D-F) cell volume, G-I) cell deformation, J-L) Young's modulus; in these graphs COVID-19 patients (yellow, n = 17) are compared to recovered donors (green, n = 14) and healthy donors (grey, n = 24). Panels C), F), I) and L) show three patients measured at two time points, during COVID-19 and after recovery; circle markers represent the median value and error bars represent the standard deviation for each patient. Statistical comparisons in C), F), I), L) were performed using linear mixed model analysis. All other statistical comparisons were done using Kruskal-Wallis test with Dunn's posthoc test. * $p < .05$, ** $p < .01$, *** $p < .001$.
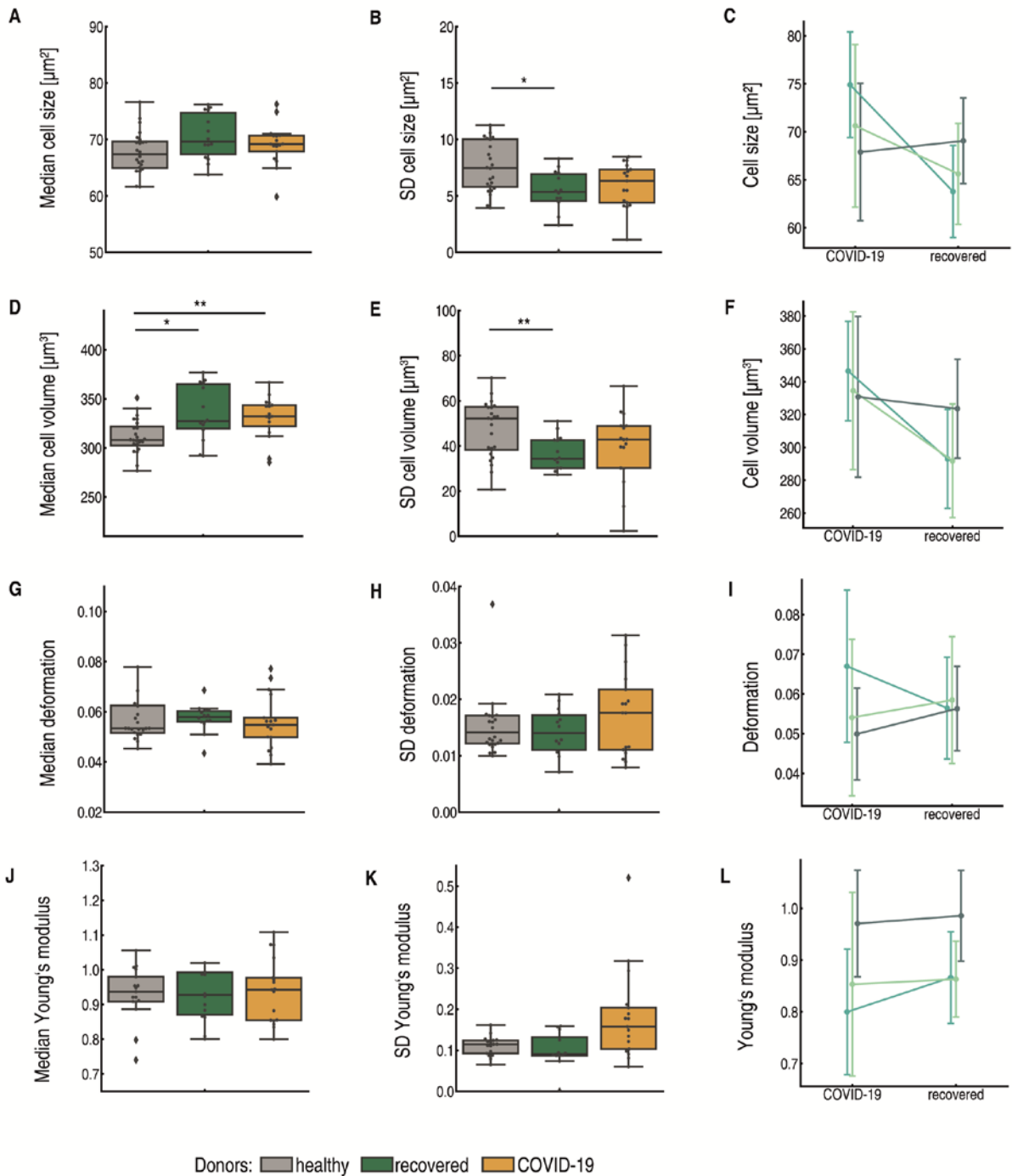
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**Supplementary figure 5. Physical properties of neutrophils of COVID-19 patients compared to controls.** Quantification of A-C) cross-sectional cell area, D-F) cell volume, G-I) cell deformation, J-L) Young's modulus; in these graphs COVID-19 patients (yellow, n = 17) are compared to recovered donors (green, n = 14) and healthy donors (grey, n = 24). Panels C), F), I) and L) show three patients measured at two time points, during COVID-19 and after recovery; circle markers represent the median value and error bars represent the standard deviation for each patient. Statistical comparisons in C), F), I), L) were performed using linear mixed model analysis. All other statistical comparisons were done using Kruskal-Wallis test with Dunn's posthoc test. * $p < .05$, ** $p < .01$, *** $p < .001$.
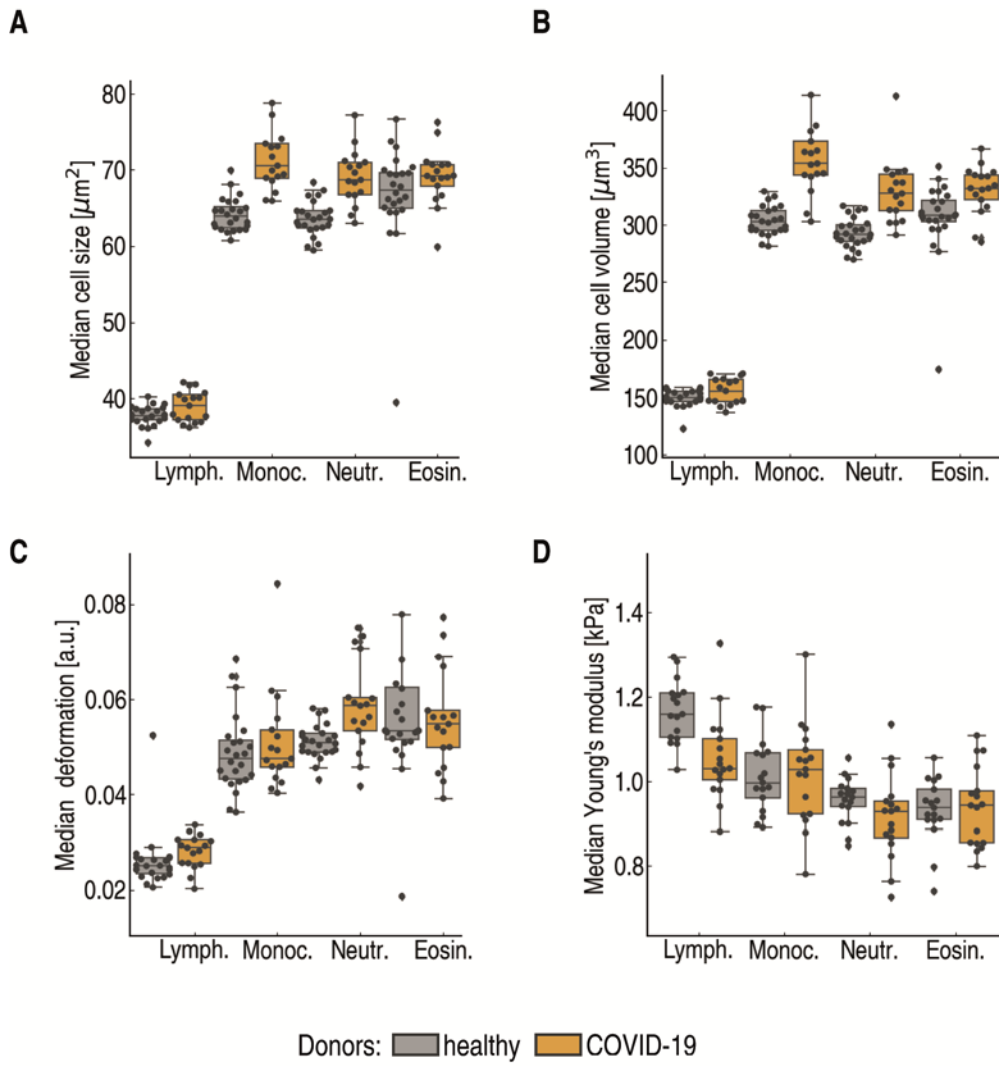
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**Supplementary figure 6. Physical properties of eosinophils of COVID-19 patients compared to controls.** Quantification of A-C) cross-sectional cell area, D-F) cell volume, G-I) cell deformation, J-L) Young's modulus; in these graphs COVID-19 patients (yellow, n = 17) are compared to recovered donors (green, n = 14) and healthy donors (grey, n = 24). Panels C), F), I) and L) show three patients measured at two time points, during COVID-19 and after recovery; circle markers represent the median value and error bars represent the standard deviation for each patient. Statistical comparisons in C), F), I), L) were performed using linear mixed model analysis. All other statistical comparisons were done using Kruskal-Wallis test with Dunn's posthoc test. * $p < .05$, ** $p < .01$, *** $p < .001$.

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**Supplementary figure 7. A comparison of the physical properties of the four examined white blood cell types in COVID-19 patients (yellow) compared to the control group (grey).** A) Median cell size, B) median cell volume, C) median deformation, D) median Young's modulus.