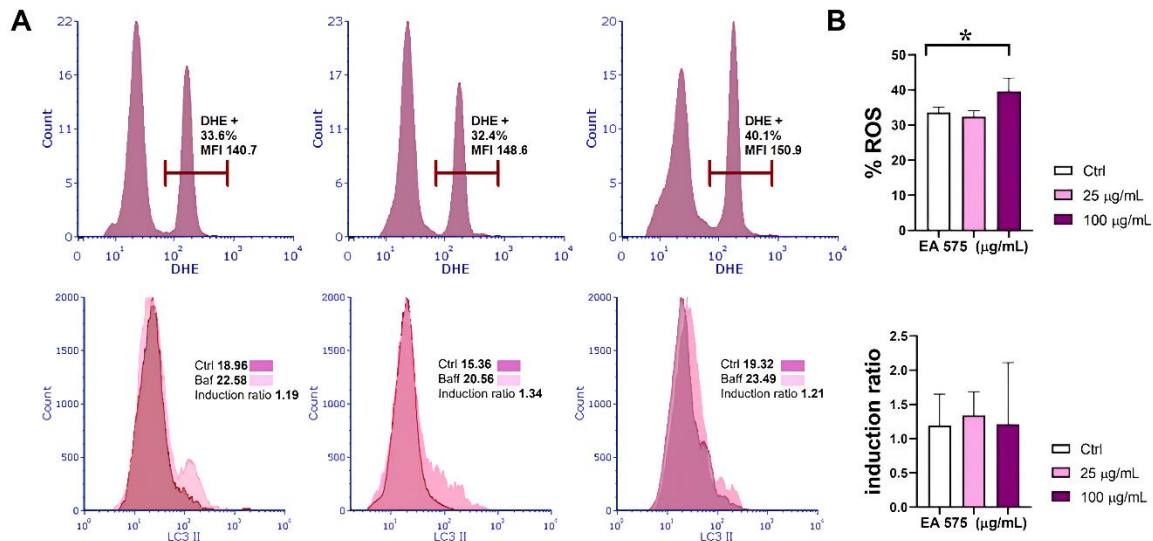


*Supplementary materials*



**Supplementary Figure S1. Upper row:**

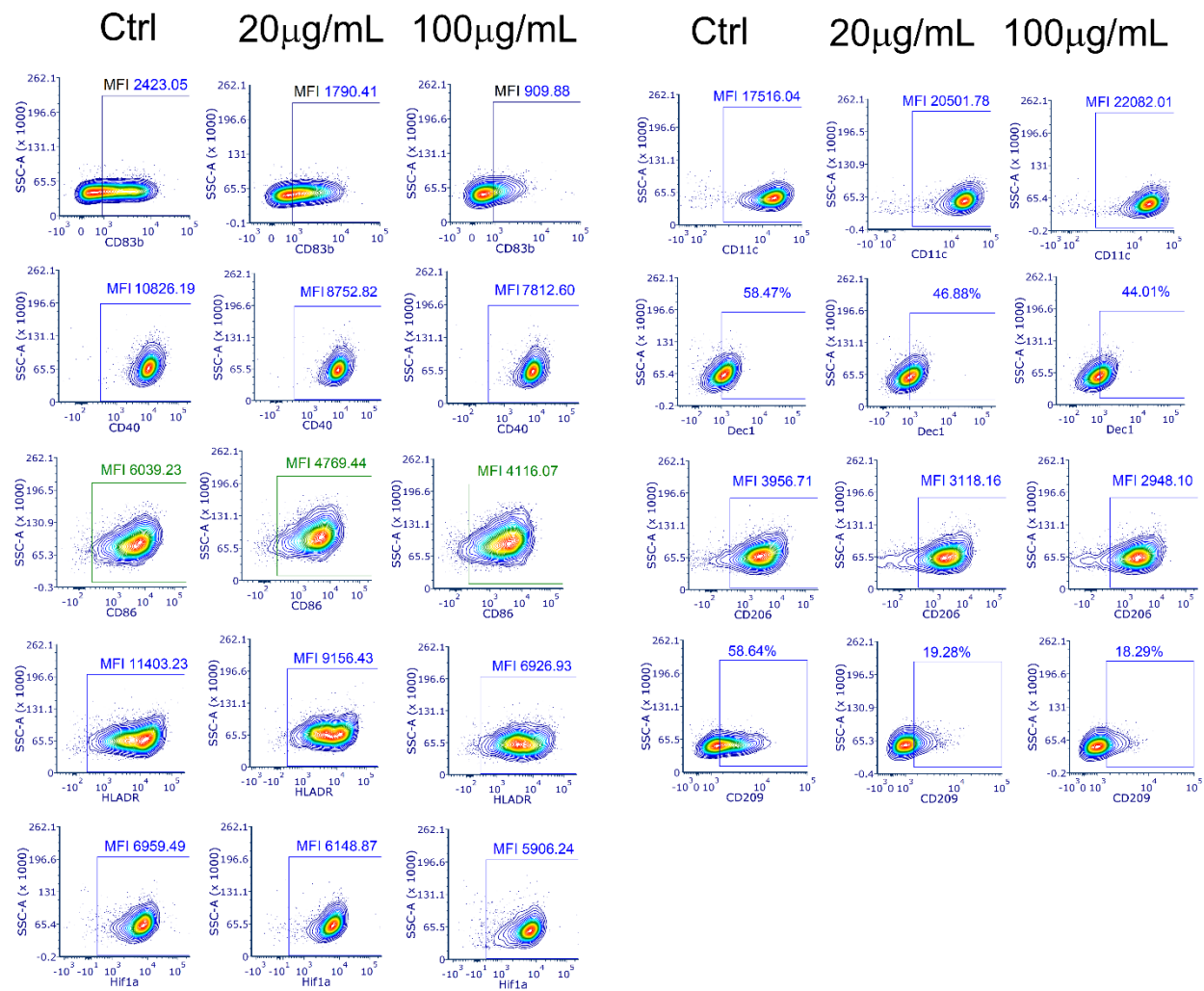
A) Expression of ROS in control monocytes induced to differentiate into imMoDCs (left) and EA 575®-treated monocytes exposed to 25 μg/mL (middle) or 100 μg/mL (right) of the extract. Histograms are shown for one representative experiment.

B) Values are expressed as the percentage of DHE+ cells (mean ± SD; n = 3). \*p < 0.05 compared to control (Ctrl).

**Bottom row:**

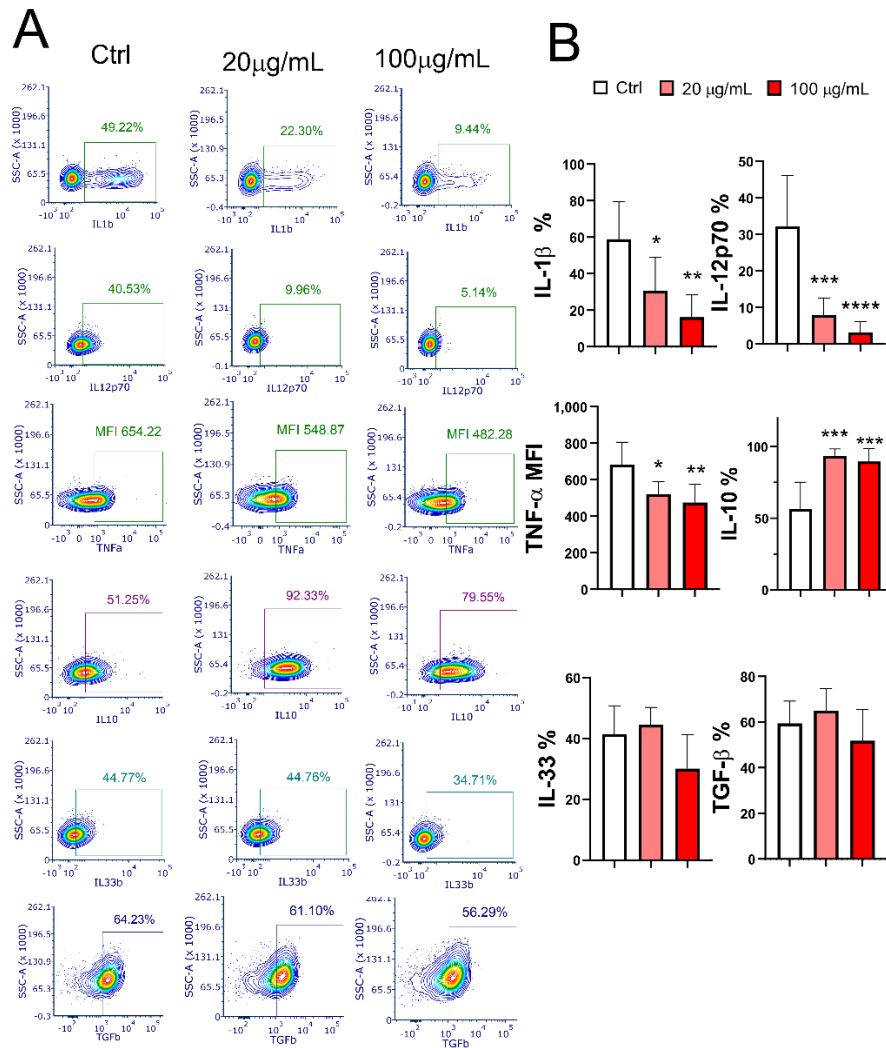
A) Autophagy in control monocytes induced to differentiate into imMoDCs (left), EA 575®-treated monocytes exposed to 25 μg/mL (middle), or 100 μg/mL (right) of the extract. Histograms of LC3II+ cells are shown for one representative experiment.

B) Induction ratios, calculated as the expression levels in the presence versus absence of bafilomycin, are presented as mean ± SD (n = 3).



**Supplementary Figure S2.** The effect of EA 575® on the expression of differentiation and maturation markers on mMoDCs

MoDCs were differentiated from monocytes in the presence of lower (20 µg/mL) and higher (100 µg/mL) concentrations of EA 575® over 4 days and subsequently induced to mature using LPS/IFN-γ. The expression of markers on mMoDCs was analyzed by flow cytometry and is displayed as individual plots from one representative experiment. Results are expressed as the percentage of marker-positive cells or as the mean fluorescence intensity (MFI).



**Supplementary Figure S3.** The effect of EA 575® on the expression of intracellular cytokines in mMoDCs

MoDCs were differentiated from monocytes in the presence of lower (20 μg/mL) and higher (100 μg/mL) concentrations of EA 575® over 4 days and subsequently induced to mature with LPS/IFN-γ. Cytokine expression in mMoDCs is presented as individual flow cytometry plots from one representative experiment (A) or as mean percentages or mean fluorescence intensity (MFI) ± SD (n = 6 donors) (B). Statistical significance compared to control mMoDCs is indicated above the bars; NS = not significant. \*p < 0.05; \*\*p < 0.01; \*\*\*p < 0.001; \*\*\*\*p < 0.0001 compared to control (Ctrl).

**Supplementary Table S1.** The effect of EA 575® on the production of cytokines by imMoDCs

| Cytokine<br>(pg/mL) | Control      | EA 575®<br>(20 µg/mL) | p  | EA 575®<br>(100 µg/mL) | p        |
|---------------------|--------------|-----------------------|----|------------------------|----------|
| IL-12p70            | 12.1 ± 6.5   | 10.2 ± 7.1            | NS | 6.2 ± 5.2              | NS       |
| IL-23               | 21.3 ± 8.5   | 22.2 ± 13.0           | NS | 19.4 ± 10.6            | NS       |
| IL-27               | 96.5 ± 18.3  | 90.4 ± 21.6           | NS | 144.8 ± 31.4           | < 0.001  |
| IL-10               | 18.3 ± 14.4  | 31.6 ± 20.6           | NS | 29.2 ± 18.8            | NS       |
| TGF-β               | 54.2 ± 21.1  | 65.2 ± 14.9           | NS | 74.0 ± 22.9            | NS       |
| IL-1 β              | 13.5 ± 6.3   | 18.2 ± 4.8            | NS | 8.9 ± 5.2              | NS       |
| TNF-α               | 19.0 ± 3.9   | 13.8 ± 3.7            | NS | 5.7 ± 4.2              | < 0.0001 |
| IL-6                | 188.4 ± 29.8 | 166.5 ± 28.6          | NS | 124.5 ± 35.7           | < 0.01   |
| IL-8                | 245.2 ± 45.2 | 324.6 ± 23.4          | NS | 126.3 ± 42.3           | < 0.0001 |

MoDCs were differentiated from monocytes in the presence of lower (20 µg/mL) and higher (100 µg/mL) concentrations of EA 575® over a 5-day period.

Cytokine levels were measured in culture supernatants and are expressed as mean concentrations (pg/mL) ± SD (n = 6 donors). NS = not significant.

**Supplementary Table S2.** Modulatory Effects of EA 575® on Cytokine Production by imMoDCs and mMoDCs

| Cytokines | EA 575® (20 µg/mL) |        | EA 575® (100 µg/mL) |        |
|-----------|--------------------|--------|---------------------|--------|
|           | imMoDCs            | mMoDCs | imMoDCs             | mMoDCs |
| IL-12p70  | Ø                  | ↓      | Ø                   | ↓      |
| IL-23     | Ø                  | ↓      | Ø                   | ↓      |
| IL-27     | Ø                  | Ø      | ↑                   | ↓      |
| IL-10     | Ø                  | Ø      | Ø                   | Ø      |
| IL-8      | Ø                  | Ø      | ↓                   | ↑      |
| TGF-β     | Ø                  | Ø      | Ø                   | Ø      |
| IL-1β     | Ø                  | ↓      | Ø                   | ↓      |
| TNF-α     | Ø                  | ↓      | ↓                   | ↓      |
| IL-6      | Ø                  | Ø      | ↓                   | ↓      |

Symbols: Ø = no effect; ↓ = decrease ; ↑ = increase