

Membrane-bound ACE and ACE mRNA transcripts in monocyte subsets of HD patients

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Introduction

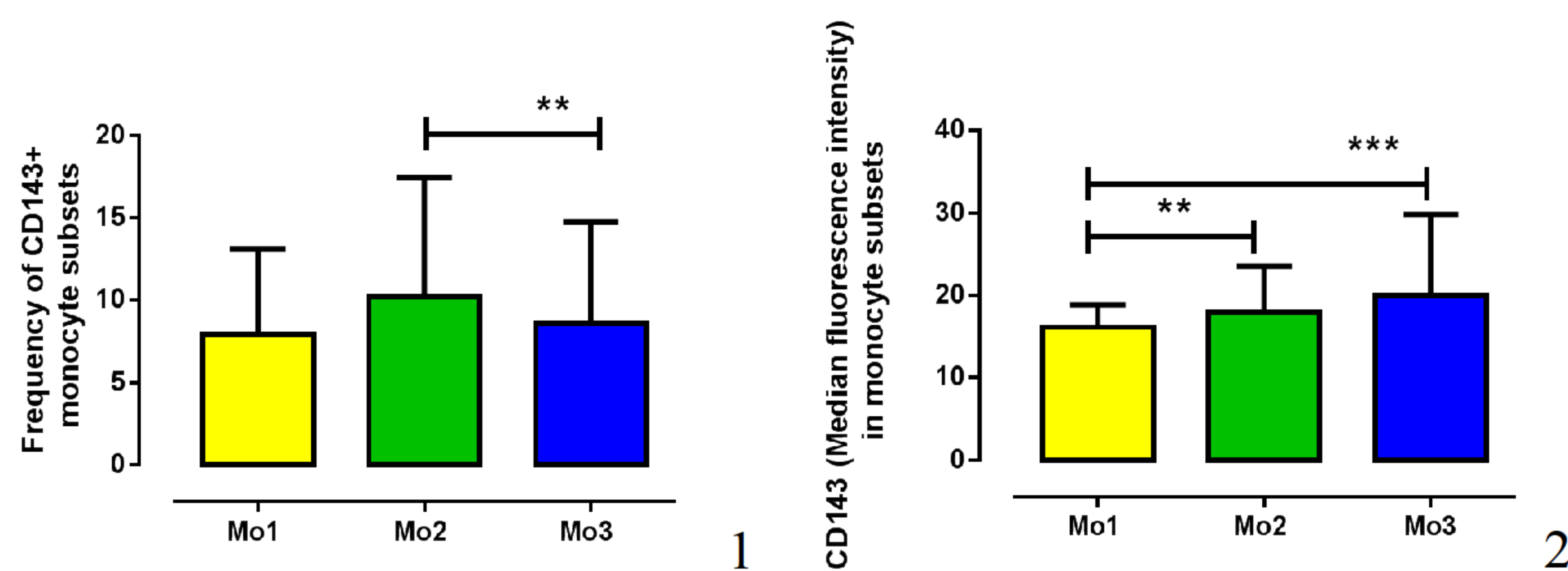
Recently membrane-bound ACE protein expression was reported to be elevated in monocytes of hemodialysis patients (HD) in comparison to healthy controls. Especially the CD14⁺⁺CD16⁺ subset (Mo2) appeared to express large amounts of ACE. Elevated Mo2 numbers in combination with high ACE expression were associated with cardiovascular disease and mortality in these patients. The relationship of membrane-bound ACE protein expression and ACE mRNA expression in isolated monocyte subsets was not investigated up to now. In 12 Dialysis patients both data sets were available.

Subjects and methods

Membrane-bound ACE was evaluated in 59 HD patients. Monocytes were isolated from 12 HD patients. The monocytes subset sorting protocol, performed on a ARIA II (BD) device, included separation of the three subsets (CD14⁺⁺CD16⁻, Mo1; CD14⁺⁺CD16⁺, Mo2; CD14⁽⁺⁾CD16⁺⁺, Mo3) after staining with anti-CD14 and -CD16 specific antibodies. Membrane-bound ACE (CD143) was detected using the anti-CD143 specific clone 9B9. The antibody staining protocol included a FcR-blocking step to prevent unspecific staining results. Isotype controls were also part of the experimental setting. RNA expression data (x-fold expression compared to healthy controls) were calculated using the formula: $2^{-(dCT(ACE\ target) - dCT(\beta\text{-actin}))/2} / 2^{-(dCT(ACE\ control) - dCT(\beta\text{-actin}))}$.

Results

Membrane-bound ACE expression in monocytes subsets of 59 HD patients

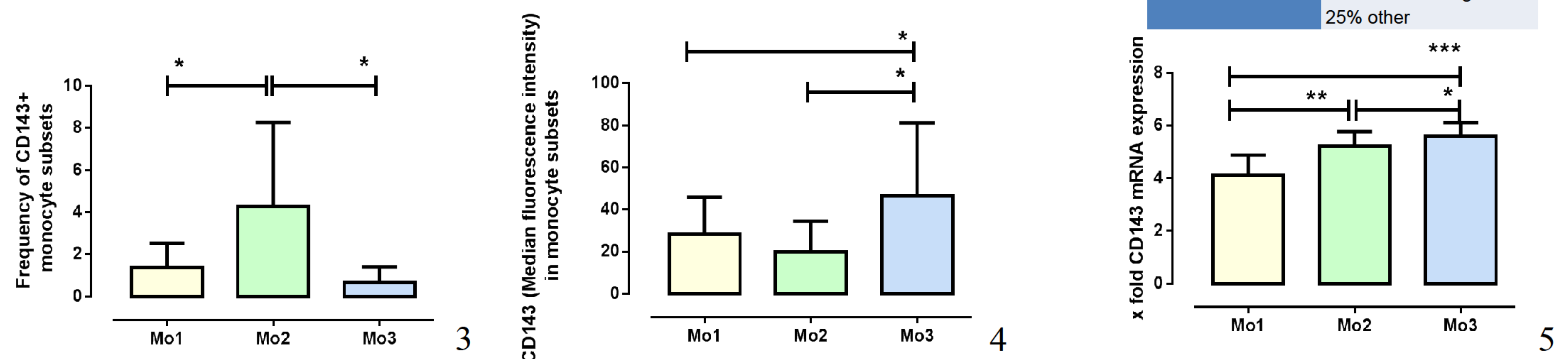


- 1) Among monocyte subsets significantly more Mo2 cells are CD143 (ACE)-positive in HD patients (N=59).
- 2) CD143 expression density is highest on Mo3 cells.
Statistics: One way ANOVA, Dunn's multiple comparisons test

Membrane-bound ACE protein and ACE mRNA expression in isolated monocytes subsets of 12 HD patients

- 3) Among monocyte subsets significant more Mo2 cells are CD143 (ACE) – positive.
 - 4) CD143 expression density is highest on Mo3 cells.
 - 5) ACE mRNA expression is elevated in isolated Mo3 cells.
- Statistics: One way ANOVA, Tukey's multiple comparisons test

Demographic data	
AGE (Years)	62.4±9.8
CRP (mg/dl)	5.2±4.1
Creatinine (µmol/L)	740.8±229.3
Urea (mmol/L)	19.6±4.3
Albumin (g/dL)	3.7±0.5
HbA1c (%)	5.8±0.9
Dialysis vintage (Years)	10.7±8.4
Gender (female, %)	50
Diabetes (%)	50
Causes of renal failure	33% Diab. Nephropathy 25% Glomerulonephritis 17% Morbus Wegener 25% other



Conclusions

The intracellular ACE machinery, especially part of Mo2 and Mo3 monocytes may a prerequisite for Ang II triggered differentiation effects towards macrophages on the one and dendritic cells on the other hand. ACE surface and mRNA expression appear to be elevated in Mo3 cells of HD patients. This is in contrast to a recently published paper*, that studied ACE1 and ACE2 expression in isolated monocytes of healthy controls.

*Rutkowska-Zapala et al. Clin xperiment Immunol 2015

