

Dysregulated Balance of CD39 and CD73 Cells in Diabetic ESRD Patients on Hemodialysis

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Introduction and Aims

CD39 and CD73 are an ecto-enzyme that degrades ATP which is a potent immune activator. CD39 and CD73 expression by regulatory T (Treg) cells contributes to the protective role in renal injury in an animal model of ischemic reperfusion injury. Recent studies demonstrate the protective anti-inflammatory role of CD39/CD73 molecules pathway during renal hypoxia.

Our previous study showed that immune response may play an role in the pathogenesis of type 2 DM with nephropathy. However, the role of CD39 and CD73 has not yet to be clarified in diabetic patients.

The aim of this study was designed to evaluate the frequency of CD39 and CD73 cells and the correlation among ROS and CD39 & CD73 in diabetic ESRD patient on hemodialysis .

Materials and Methods

- Subjects** ; Fifteen diabetic ESRD patients receiving hemodialysis and 15 healthy controls were recruited.
- Methods** ; Peripheral blood mononuclear cells were collected and stained with antibodies to CD4, CD25, FOXP3, CD39 and CD73. The balance of CD39/CD73 Treg cells were measured by using flow cytometry. Intracellular reactive oxygen species (ROS) generation was measured by flow cytometry using fluorescent dye, H2DCF-DA.

Results

1. Characteristics of the Subjects

	Healthy Controls	Diabetic ESRD	P
Number (n)	15	15	1.00
Age (yr)	45.0±3.1	61.8±3.0	<0.02
Sex (male:female)	10:5	9:6	>0.05

2. Frequency of Treg. (Fig-1)

Diabetic ESRD patients had an increased frequency of Treg (HC vs. ESRD, 3.3±0.4 vs. 10.7±3.0, $p=0.038$).

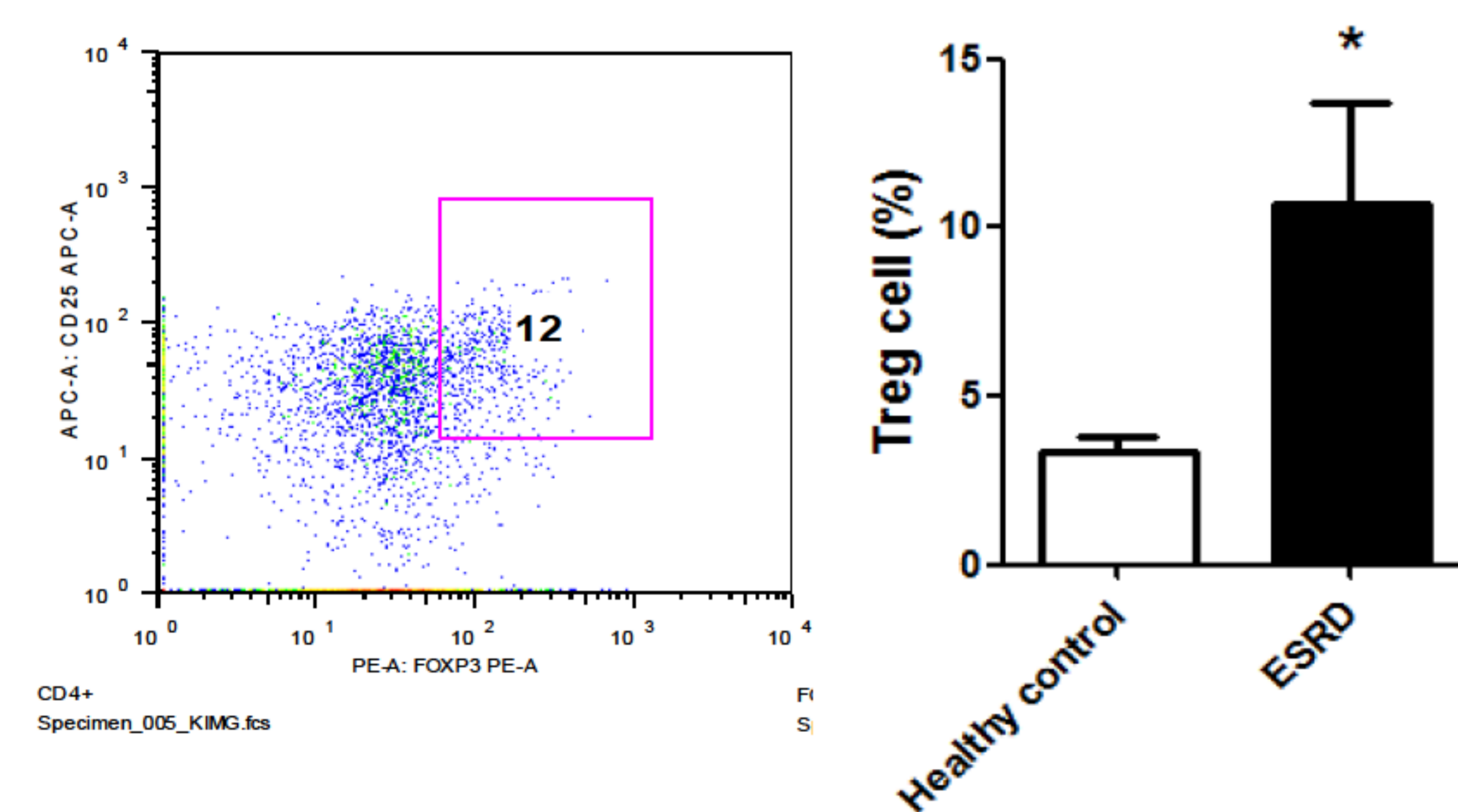


Fig-1. Frequency of Treg cell.

3. Frequency of CD39 & CD73 cells. (Fig-2)

Diabetic ESRD patients had an increased frequency of CD39 cells (HC vs. ESRD, 13.0±4.1 vs. 33.8±5.7, $p=0.012$) and a decreased frequency of CD73 cells (HC vs. ESRD, 10.3±1.8 vs. 6.2±0.8, $p=0.04$).

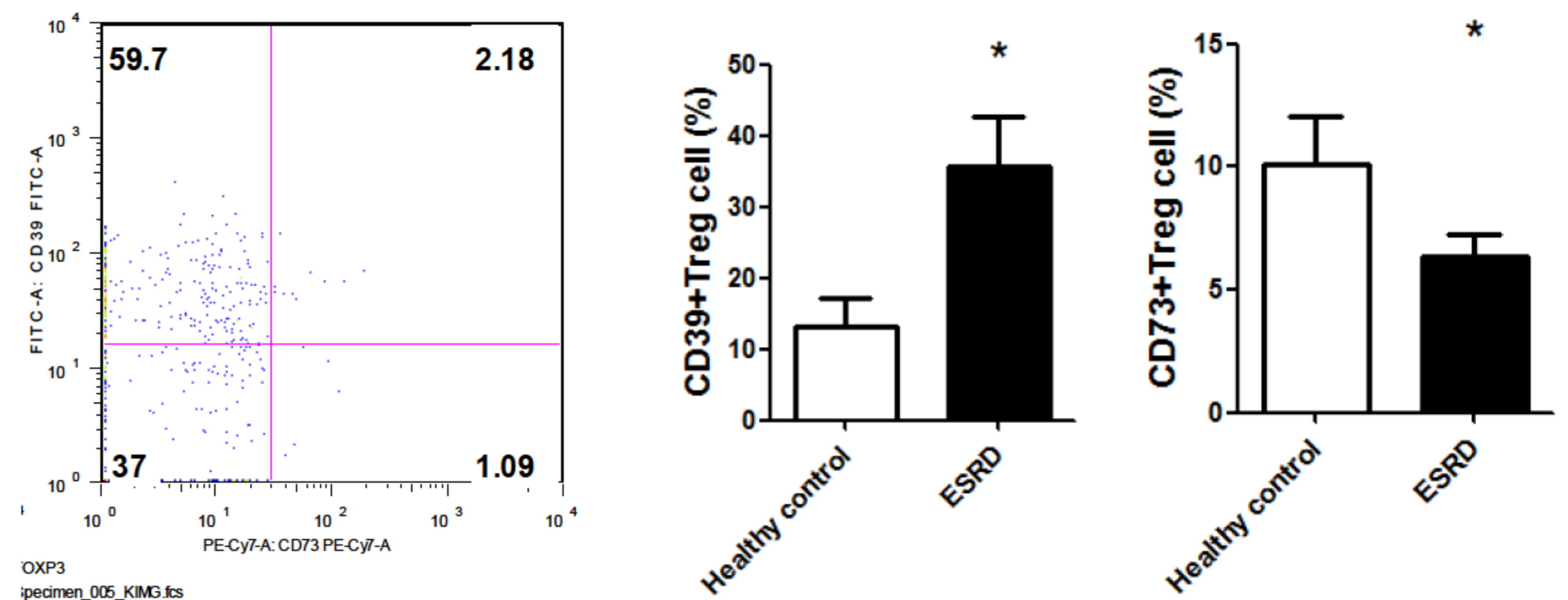


Fig-2. Frequency of CD39 and CD73 on Treg cell.

4. CD39/CD73 Ratio (Fig-3)

The ratio of CD39/CD73 was markedly decreased in diabetic ESRD patients (HC vs. ESRD, 1.4±0.5 vs. 0.3±0.1, $p=0.01$).

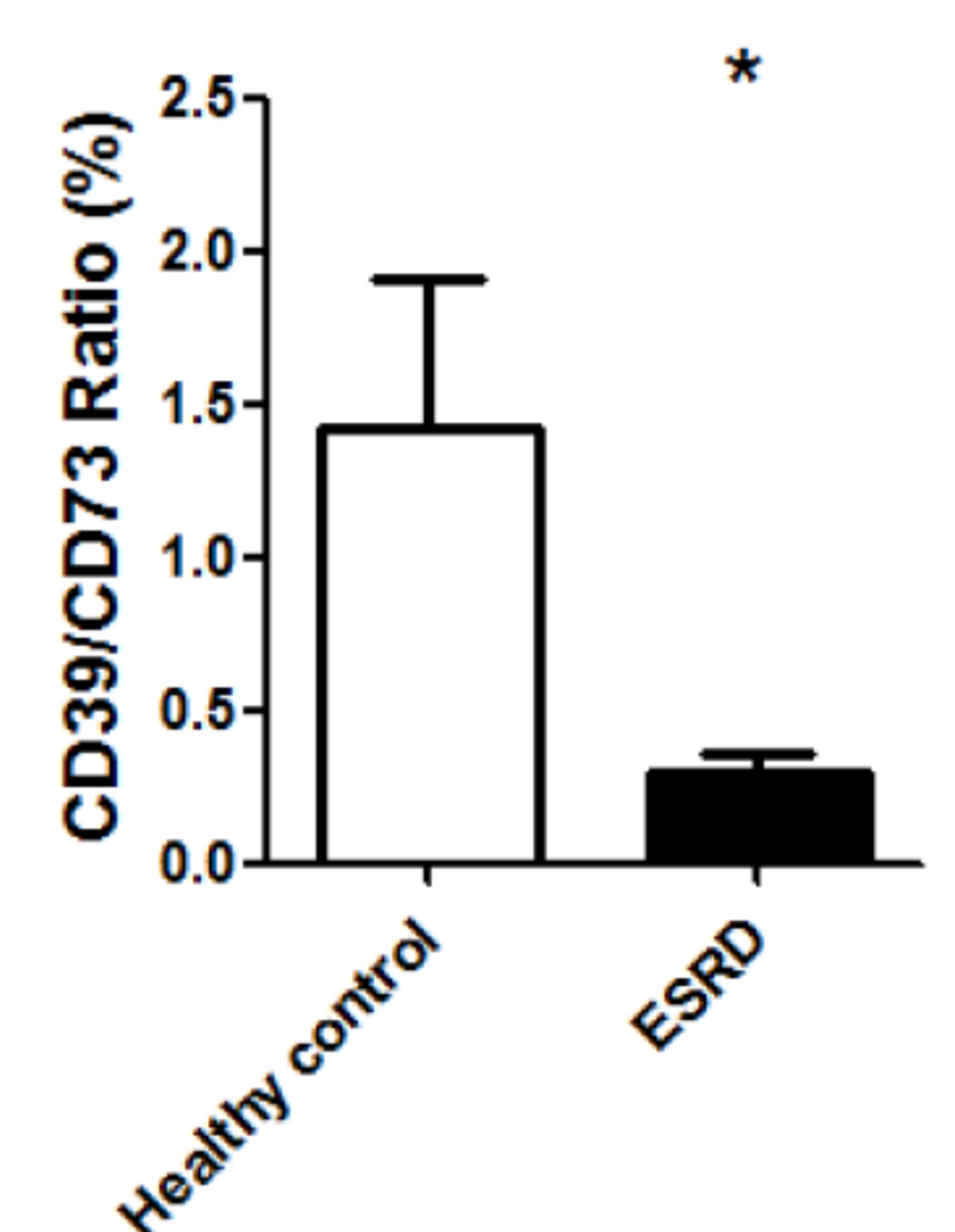


Fig-3. CD39/ CD73 ratio of Treg cells.

5. Reactive oxygen species (Fig-4)

Cellular reactive oxygen species (ROS) were markedly increased in ESRD patients, but was not revealed in healthy control (HC vs. ESRD, 8.2±1.9 vs. 48.6±6.2, $p<0.001$).

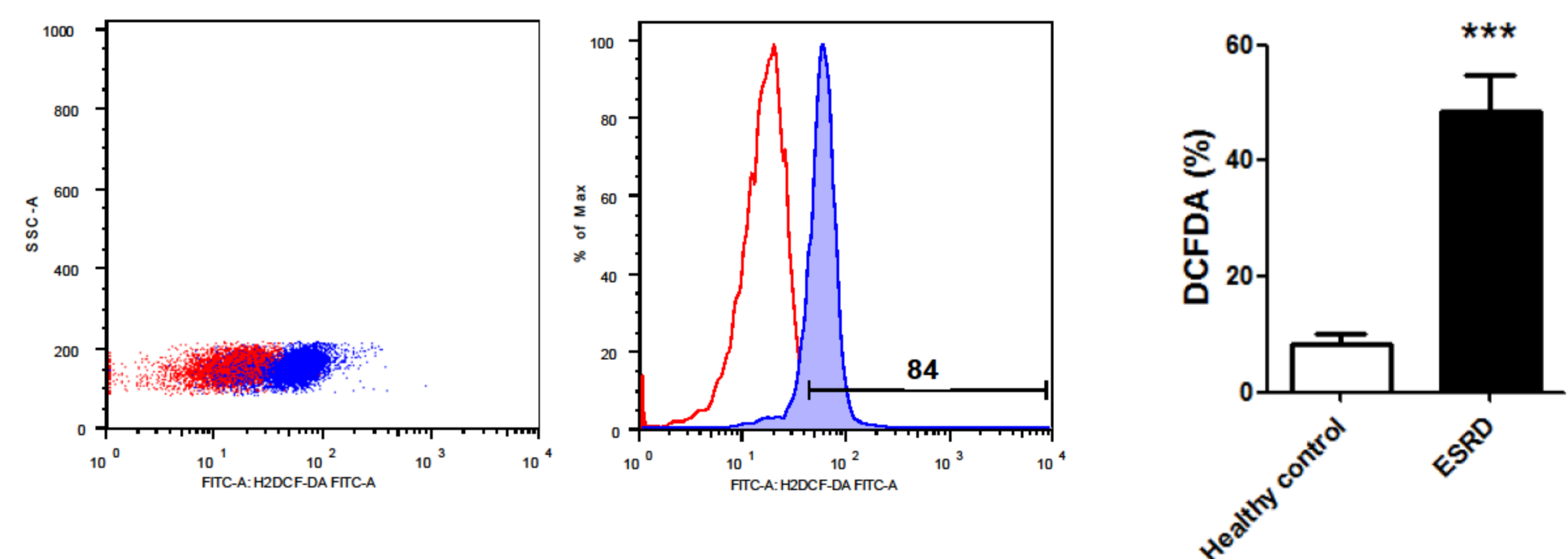
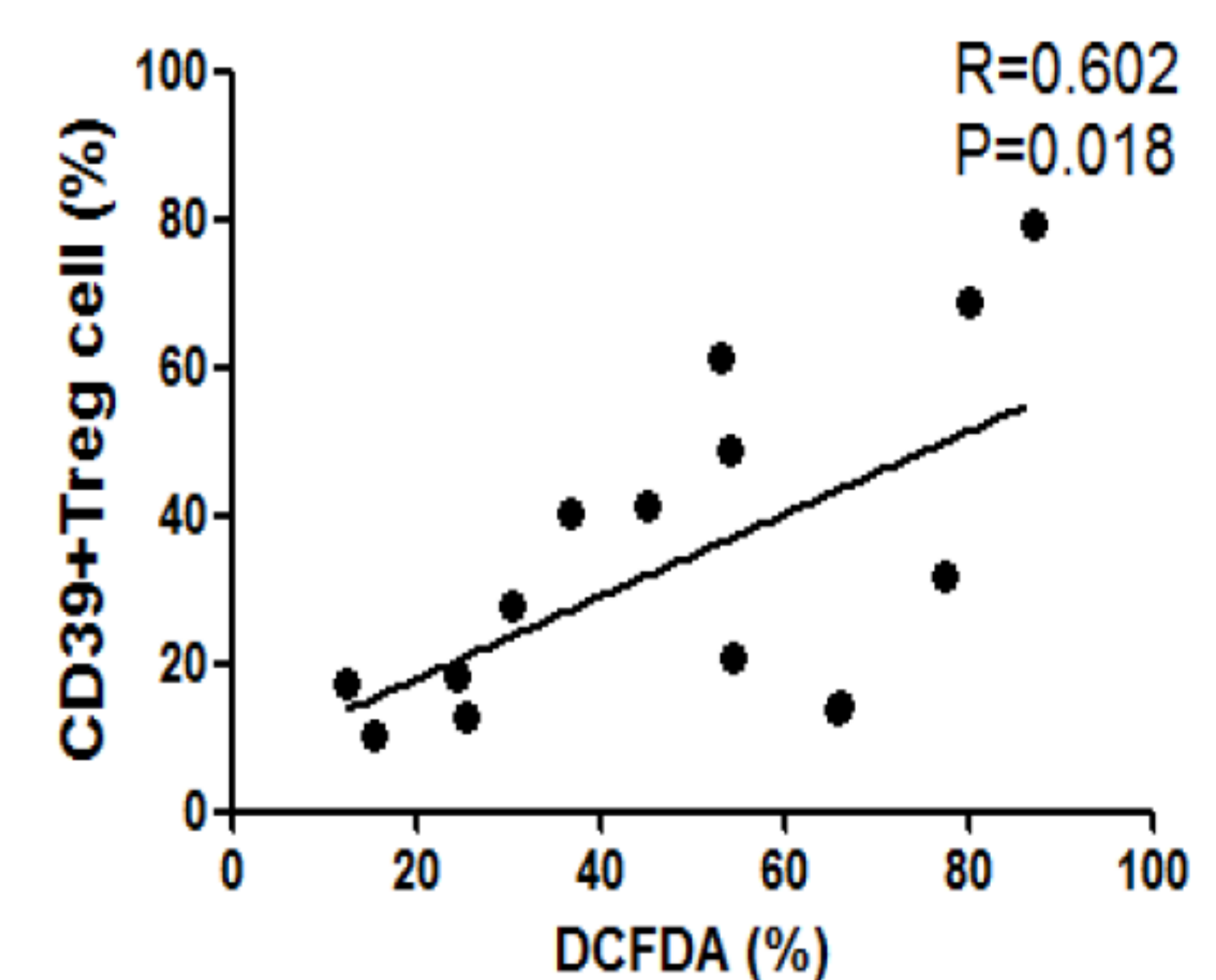


Fig-4. Increased ROS level in diabetic ESRD patients.

6. Correlation of ROS and CD39

Diabetic ESRD patients showed a positive correlation between the frequency of ROS and CD39 cells. ($r=0.602$, $p=0.018$).

Fig-5. Correlation of ROS and CD39.



Conclusions

Diabetic ESRD patients showed increased the frequency of Treg cells and decreased CD39/CD73 ratio. In addition, ROS was increased and correlated with CD39 in diabetic ESRD patients on hemodialysis. These results suggests that CD39/CD73 cells may play an role in the immune response of diabetic ESRD patients on hemodialysis.

