Mitochondrial Dysfunction in Podocyte Reduces Alpha Actinin-4 and Synaptopodin in Podocyte, Which Induces Proteinuria

Dae Eun Choi[1], Jin Young Jeong[1], Yoon Kyung Chang[2], Ki-RyangNa[1], Kang Wook Lee[1], and Young-Tai Shin[1]

Renal Division[1], Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Rebubric of Korea, Department of Internal Medicine[2], Daejeon Saint Mary Hospital, Daejeon, Repubric of Korea

OBJECTIVES

Our previous report showed that Crif1 deletion induce severe mitochondrial destruction in mice podocyte. There results induce massive albuminuria and effacement of foot process in mice. Actin cytoskeleton architecture and dynamics in podocyte are important constituents of the glomerular filtration barrier. There have been few studies about relation of mitochondria and actin cytoskeleton in podocytes of glomerulus. We evaluated the changes of actin cytoskeletal proteins and artchitecture in mitochondrial injured podocyte.

METHODS

We used immortalized mouse podocyte cell line. Crif1 silencing(si) RNA treatment was used for inducing mitochondrial injury. We divided podocytes into 3 groups; control podocytes, scrumble(sc) RNA treated podocytes, and Crif1 siRNA treated podocytes. We checked the expression of mitochondrial respiratory complex I~V, WT-1, and Crif1 for mitochondrial dysfunction in immortalized podocyte. We evaluated the expression of alpha actinin-4, synaptopodin, nephrin, ZO-1, and colfillin using western blot. Using confocal microscopy, we examined actin cytoskeleton architecture and mitochondria of podocyte. For evaluation of cell migration, we performed scratch assay.

RESULTS

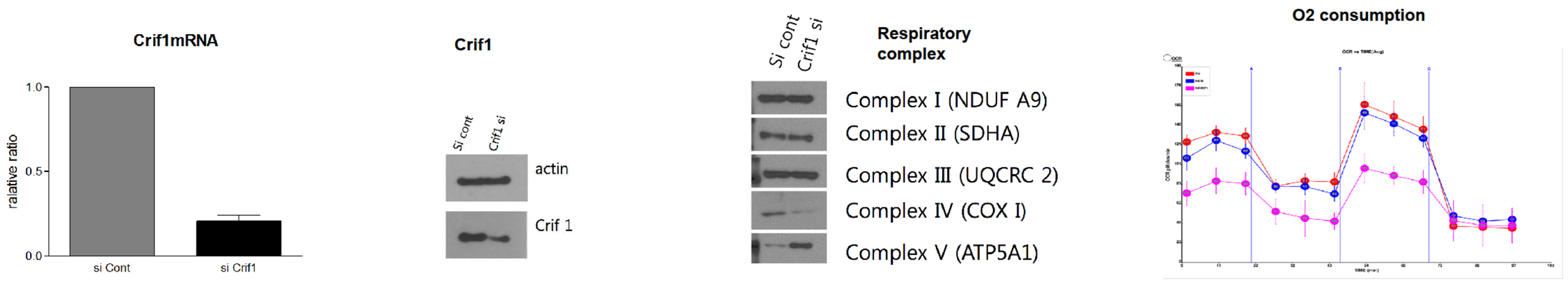

Figure 1. Crif1 siRNA treatment reduced the level of Crif1 mRNA expression and Crif1 protein in cultured podocytes. Crif1 siRNA treatment reduced the expressions of mitochondrial respiratory complex IV and O_2 consumption in cultured podocytes.

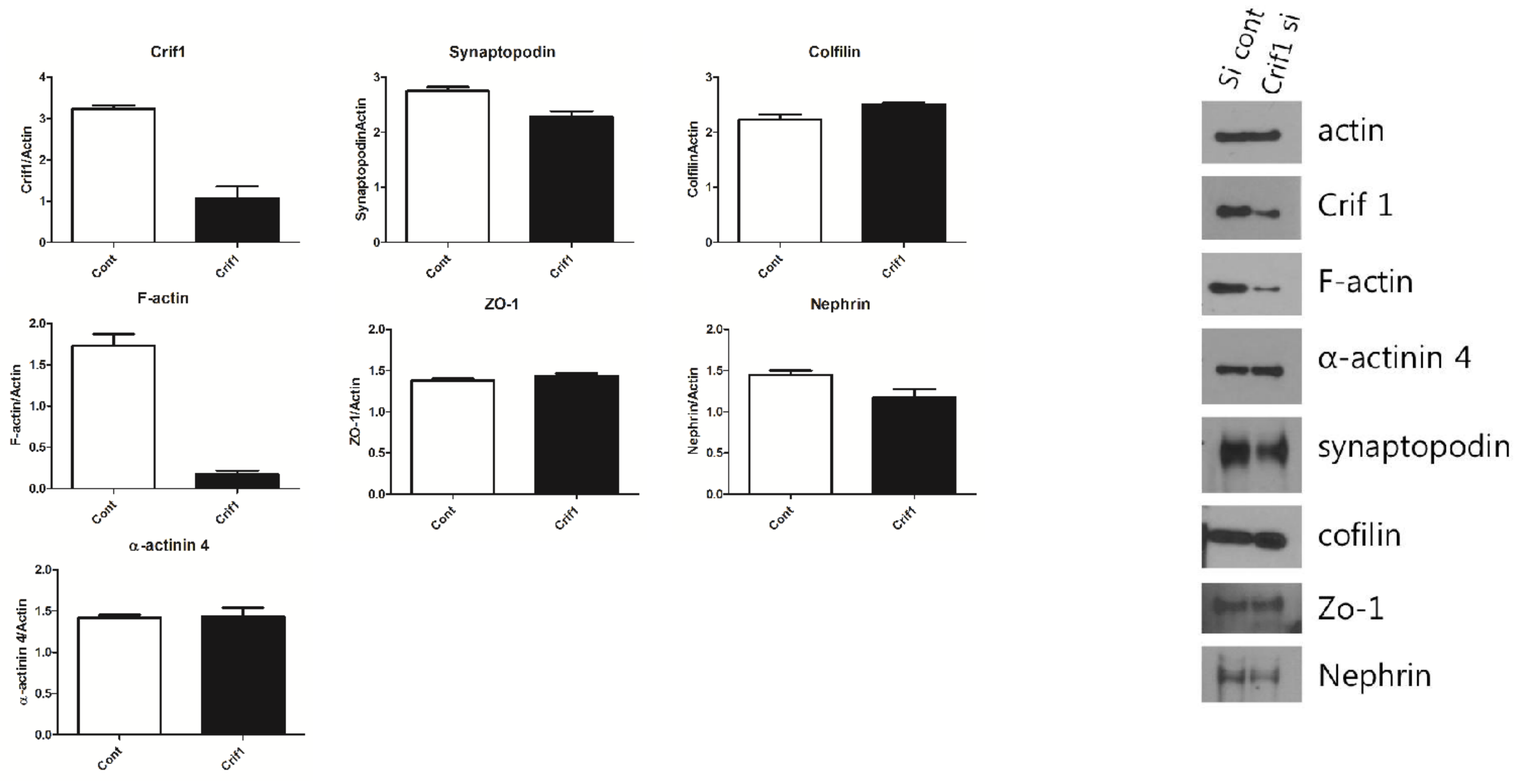

Figure 2. Alpha actinin-4 were significantly decreased in Crif1 siRNA treated podocyte compared to control and Crif1 scRNA treated podocytes. There were no differences in nephrin and ZO-1. Crif1 siRNA treated podocyte showed an enhanced formation of dot-like alpha actinin-4 and an increase of fragment mitochondria in confocal microscopy compared to scRNA treated podocyte.

CONCLUSIONS

With the above results, it is speculated that mitochondrial dysfunction induced by crif1 inhibition reduces alpha actinin-4 and synaptopodin in podocyte.