

# KSN 2016 Abstract Submission

*CKD & associated complications*

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## Fucoidan Improves Bioactivity and Vasculogenic Potential of Mesenchymal Stem Cells in Murine Hind limb Ischemia associated with Chronic Kidney Disease

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**Background:** Chronic kidney disease (CKD) is a significant risk factor for cardiovascular and peripheral vascular disease. Although mesenchymal stem cell (MSC)-based therapy is a promising strategy for treatment of ischemic diseases associated with CKD, the associated pathophysiological conditions lead to low survival and proliferation of transplanted MSCs.

**Methods:** We investigated the effects of fucoidan, a sulfated polysaccharide, on the bioactivity of adipose tissue-derived MSCs and the potential of fucoidan-treated MSCs to improve neovascularization in ischemic tissues of CKD mice.

**Results:** Treatment of MSCs with fucoidan increased their proliferative potential and the expression of cell cycle-associated proteins, such as cyclin E, cyclin dependent kinase (CDK) 2, cyclin D1, and CDK4, via focal adhesion kinase and the phosphatidylinositol-4,5-bisphosphate 3-kinase/Akt axis. Moreover, fucoidan enhanced the immunomodulatory activity of MSCs through the ERK-IDO-1 signal cascade. Fucoidan was found to augment the proliferation, incorporation, and endothelial differentiation of transplanted MSCs at ischemic sites in CKD mice hind limbs. In addition, transplantation of fucoidan-treated MSCs enhanced the ratio of blood flow and limb salvage in CKD mice with hind limb ischemia.

**Conclusion:** In conclusion, fucoidan contributes to the proliferative potential of MSCs via the FAK and PI3K-Akt signal cascade and enhances their immunomodulatory property through the ERK-IDO-1 axis, resulting in facilitation of neovascularization by fucoidan-activated MSCs in ischemic tissues of CKD mice. These findings suggest that fucoidan-treated MSCs may be used as a novel strategy to address ischemic diseases in patients suffering from several chronic diseases.

**Keywords:** Chronic kidney disease, Fucoidan, Ischemic disease, Mesenchymal stem cells, Neovascularization, Vascular repair