

Abstract Submission No. : 2130

Immunohistochemical Expression of Orai1 in Human Diabetic Nephropathy and Its Significance for Prognosis and as Therapeutic Target

Yoojin Kwak¹, Hanwul Shin², Junyoung Lee², Jaeseok Kim², Jaewon Yang², Byoung-Geun Han², Seung-Kuy Cha³, Minseob Eom¹

¹Department of Pathology, Yonsei University Wonju College of Medicine, Korea, Republic of

²Department of Nephrology, Yonsei University Wonju College of Medicine, Korea, Republic of

³Department of Physiology, Yonsei University Wonju College of Medicine, Korea, Republic of

Objectives:

Diabetic nephropathy (DN) is a representative disease that causes about half of all end-stage renal disease in world. However, the attempts for targeted therapy for DN have been lacking to date. Store-operated Ca²⁺ entry (SOCE) is a primary Ca²⁺ influx mechanism in non-excitable cells that is mediated by pore-forming subunit Orai1 and ER Ca²⁺ sensor STIM1. Currently, it has been argued whether Orai1 overexpression protects or aggravates against renal pathologies. Here, we investigate the significance of Orai1 expression with clinico-pathological parameters in human DN patients.

Methods:

Ninety-three patients diagnosed with DN from 2009 to 2019 were enrolled and immunohistochemical staining for Orai1 was performed using paraffin blocks (figure). The Renal Pathology Society DN classification (RPS class) and various clinical parameters were compared with Orai1 expression. The results were compared by dividing them into a glomerulus (G) and tubulo-interstitium (T-I).

Results:

In T-I, Orai1 was overexpressed in DN compared to the control group, and Orai1 expression was significantly correlated with higher RPS class and higher interstitial fibrosis and tubular atrophy score ($p < 0.001$). While Orai1 expression was positively correlated with serum creatinine and chronic kidney disease (CKD) stages, estimated glomerular filtration rate and HbA1c were inversely associated with Orai1 expression ($p < 0.001$). In univariate logistic regression analysis, Orai1 is significantly correlated with high RPS class and advanced CKD. In multivariate logistic regression analysis, Orai1 is also confirmed as a significant risk factor for advanced CKD ($p = 0.002$). The result of G was also similar to that of T-I.

Conclusions:



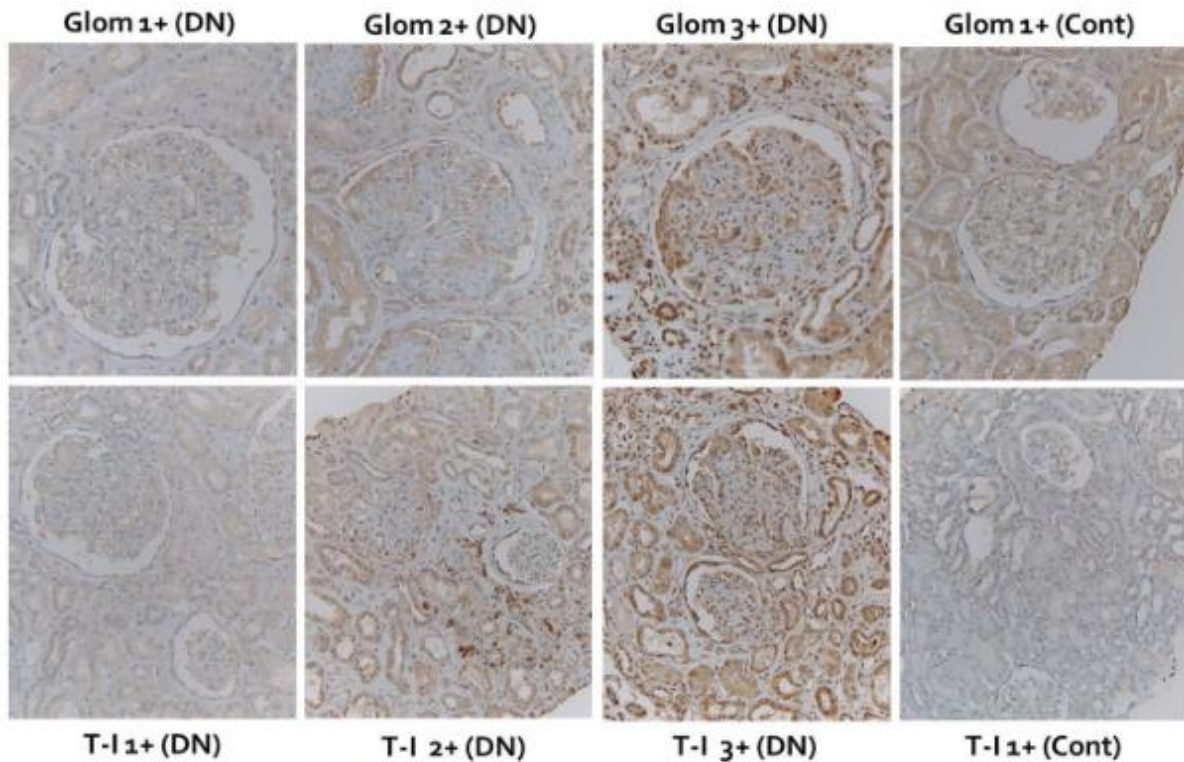
KSN 2021

FULLY VIRTUAL MEETING

 September 02 (Thu) - 05 (Sun)

Taken together, our results suggest that Orai1 is well correlated with histologic and clinical severity of DN. Therefore, Orai1 could be used as a valuable marker to evaluate DN condition and to predict the prognosis of DN. Moreover, Orai1 could provide a clue of novel therapeutic target for DN in future.

Figure. The result of immunohistochemical stain for Orai-1 in diabetic nephropathy



Glom, glomerulus; DN, diabetic nephropathy; Cont, control; T-I, tubulo-interstitium

Table. The correlation between Orai-1 expression and CKD stage in DN (Multivariate logistic regression)

Adjustments	Parameters	Odds ratio	95% Confidence interval		p-value
			Lower limit	Upper limit	
Age, sex, BMI, HbA1c,	Orai-1 (G)	11.208	2.590	48.497	0.001
DM duration, and HTN	Orai-1 (T-I)	13.876	2.694	71.476	0.002

BMI, body mass index; HTN, hypertension; G, glomerulus; T-I, tubulo-interstitium