Soluble (Pro)renin Receptor Levels in Patients with Graves' Disease

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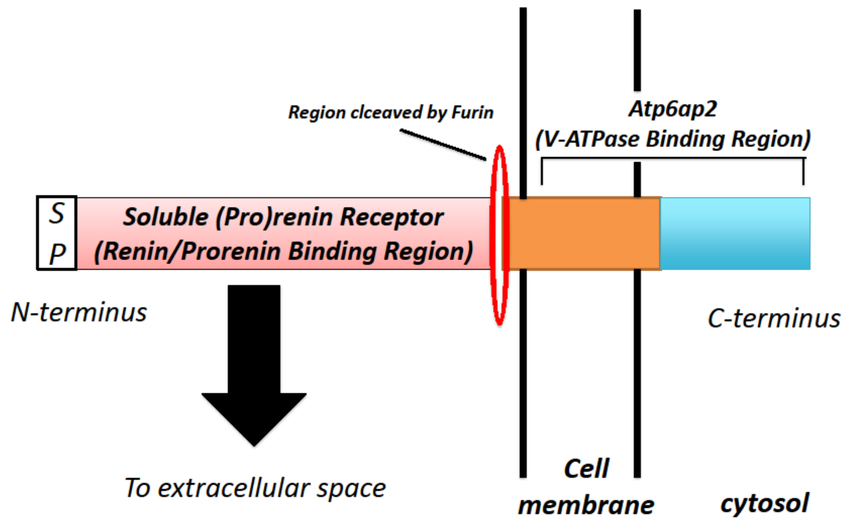
Background

The (pro)renin receptor ([P]RR) is a receptor for renin and prorenin, which regulates the tissue Renin-Angiotensin System(RAS). (P)RR also plays an important role in the assembly and function of vacuolar H^+-ATPase (V-ATPase), an ATP-dependent proton pump that transports protons across plasma membranes and acidifies intracellular compartment.

(P)RR is cleaved by furin to generate soluble (P)RR [s(P)RR], which is secreted into blood and urine. Recently , we developed s(P)RR ELISA kit to measure the concentration of s(P)RR in blood. We previous reported that high blood concentration of s(P)RR indicates poor organ prognosis in gestational diabetes, chronic renal disease(CKD) and malignant tumor.



Structure of (P)RR

Purpose

The regulating factor of (P)RR and s(P)RR remains unclear.
Thyroid hormone(TH) directly activate RAS, which suggests that TH might be one of the regulating factor of (P)RR.
Therefore, this study was conducted to investigate the relationship between thyroid function and blood s(P)RR levels in GD patients.

Methods

Study in endocrine disease patients

2012.4.1～2015.10.1
61 Untreated Graves' Disease(GD), 23 Hashimoto disease,
59 normal subject, 16 acromegaly, 13 pheochromocytoma

<Measured parameter>
Serum s(P)RR*,height, body weight, BMI, blood pressure, BUN, Cr, FT4, FT3, TSH, TRAb HbA1c, blood sugar level LDL-C, HDL-C, TG

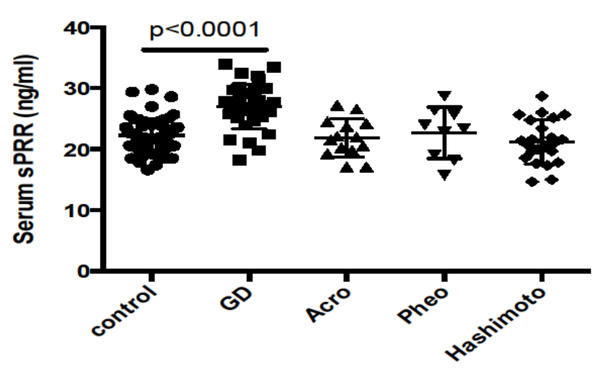
*Serum s(P)RR is measured in the early morning after 15 minutes of sitting position.

<Excretion criteria>
CKD G3～
Diabetes mellitus
Malignant tumor
Patients taking RAS inhibitor
Other severe complication

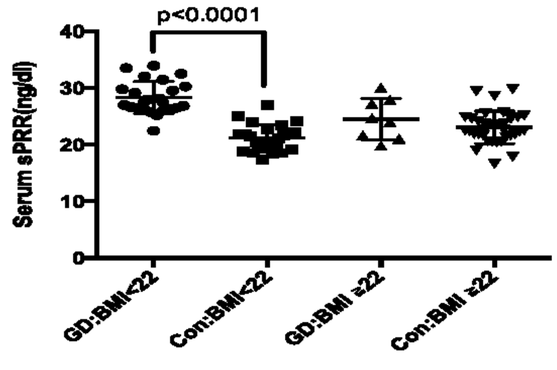
Reexamination in 6-18 month after treatment

Results

s(P)RR levels in endocrine disease patients



s(P)RR levels in GD patients



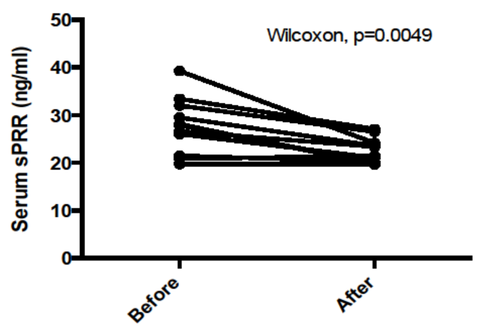
Background of GD patients

	GD (n=49)	Control (n=59)	P
Sex ratio(male:female)	13:36	15:44	
Age	47.45 ± 2.70	49.68 ± 3.51	0.61
BMI (kg/m²)	21.30 ± 1.13	22.64 ± 0.52	0.22
SBP (mmHg)	117.1 ± 2.94	122.8 ± 2.81	0.195
DBP (mmHg)	67.71 ± 2.21	75.5 ± 2.66	0.031
TSH (IU/l)	<0.005	2.17 ± 0.45	<0.0001
FT4 (ng/ml)	4.97 ± 0.36	1.18 ± 0.05	<0.0001
FT3 (pg/ml)	17.27 ± 1.63	2.83 ± 0.12	<0.0001
Cr (mg/dl)	0.51 ± 0.03	0.71 ± 0.38	0.0004
eGFR (ml/min/1.73m²)	124.2 ± 12.18	80.59 ± 3.80	0.0007
HbA1c (NGSP:%)	5.57 ± 0.09	5.25 ± 0.12	0.049
TG (mg/dl)	81.31 ± 7.14	82.57 ± 7.7	0.90
LDL-C (mg/dl)	68.80 ± 5.62	106.5 ± 6.05	<0.0001
HDL-C(mg/dl)	57.31 ± 5.83	77.0 ± 5.20	0.018

Single correlation between s(P)RR and other factors

	r	P
Age	0.104	0.59
BMI	0.002	0.75
FT4	0.357	0.044
FT3	0.349	0.050
TRAb	0.184	0.33
eGFR	0.342	0.25
HbA1c	0.262	0.32
LDL-C	0.059	0.82
HDL-C	0.454	0.078
TG	-0.516	0.019

s(P)RR level change after treatment



Multiple regression analysis with s(P)RR level

	model1 β	model1 p		model2 β	model2 p
TG	-0.047	0.056	TG	-0.047	0.047
FT4	1.089	0.428	FT4	1.026	0.146
FT3	-0.016	0.956	FT3	-	-

Treatment resistance in GD patients

	Treatment resistance	Treatment response	
Serum s(P)RR ≧27 ng/ml	11	10	21
Serum s(P)RR ＜27 ng/ml	2	8	10
	13	18	31

Treatment response: Patients in euthyroid state after 6-18 month of treatment
Treatment resistance: Patients still in hyperthyroid state after treatment

Relative Risk 2.62

Summary

1) Serum s(P)RR levels were significantly higher in GD patients than normal subjects.
2) GD patients with high s(P)RR levels showed treatment-resistance.
3) GD patients with low BMI showed higher levels of serum s(P)RR than those with high BMI, while serum s(P)RR levels were positively correlated with BMI in normal subjects.

Conclusion

These results showed that poor nutritional condition caused by GD might induce s(P)RR production to cause organ damages.

Conflict of Interest

We have no conflict of interest with regard our presentation.

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