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Insulin resistance and impairment of vascular dilatation caused by high-salt induced hypertension in FRET construct transgenic mice.

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Summary

Vasodilatation caused by insulin activates three insulin acceptor → IRS protein phosphorylation → PI - kinase (increase) → Akt activation → eNOS activation → NO of quantity of PI3,4,5-P3 increases, and it is assumed that I go through the mechanism that I called cGMP increase.) On the other hand, for insulin-resistance by salt sensitivity high blood pressure, aggravation of vasodilatation malfunction or arteriosclerosis is caused, but it is not almost clarified which stage the signal mentioned above is affected at in various blood vessels such as a heart, the aorta, a capillary, a blood vessel in a kidney. Therefore we tried development of the system which we passed through signal transmission in a single cell in the living body with FRET and could detect for time.

I made the fluorescence sensor which measured mechanism of each stage of vasodilatation by insulin. These fluorescence sensors are made including CFP and YFP both so that the fluorescence of 535 nm by FRET is detected by a change of the structure when CFP and YFP approach it.

These fluorescence sensors were overexressed PC12 cell or HepG2 cells using adenovirus vectors and were able to confirm expression with Western blotting method and a fluorescent microscope. In addition, I stimulated the cells which developed these fluorescence sensors with NGF or insulin and measured FRET. As a result, the FRET levels of IRS protein phosphorylation, PI 3- kinase activity were obseareved to increase by each stimulation from about 1.5 - 2 times for time, respectively.

We succeeded in development of the fluorescence sensor which used FRET this time. In addition, we have reported the forward examinations about insulin resistance mechanism in a various high salt food load rat or vascular lesion by RELM β till now. Using these fluorescence sensors, we are going to push forward analysis of these models more in future.