Molecular basis on the feto-maternal network in pregnancy-associated diseases

Akiyoshi FUKAMIZU

(Graduate School of Environmental and Life Sciences, University of TSUKUBA, Professor)

[Outline of survey]

One of most vexing problems of pregnancy, is a condition known as pregnancy-induced hypertension (PIH). Developing in the last trimester, PIH can send the expectant mother 's blood pressure rocketing, damaging her kidney, liver, heart, and putting both her life and that of the child she is carrying at risk. No one still knows what causes PIH, which affects up to 10% of human pregnancy and causes the majority of pregnancy-related complications. The primary function of the placenta is to act as an interface between mother and fetus that allows, and even promotes, fetal growth and development, and to contribute to the maternal cardiovascular adaptations for pregnancy. Disturbance of the normal circulatory adaptation is a core predictor of abnormal pregnancy, but despite numerous research efforts, the molecular basis underlying the regulation in the feto-maternal interface remains unclear. In this project, we focus on the molecular basis on the feto-maternal network in pregnancy-associated complications.

[Expected results]

Our previous studies in an animal model, which mated transgenic mice expressing human renin-angiotensin system components, renin and angiotensinogen, demonstrated that a paternally derived human renin produced in the placenta is secreted into the maternal circulation, resulting in the development of hypertension, cardiac and placental abnormalities, and intrauterine growth retardation, mediated by angiotensin type 1a receptor in late pregnancy. In principle, this type of transgenic condition is applicable not only to hypertension during pregnancy, but to any pregnancy-associated disease that is induced by the combination of fetal and maternal factors. Therefore, our novel approach may be useful for the molecular dissection of the pathophysiology underlying pregnancy-associated hypertension and may lead to new treatment for the complications during pregnancy.

[References by the principal researcher]

• Ishida, J., Hashimoto, T., Hashimoto, Y., Nishiwaki, S., Iguchi, T., Harada, S., Sugaya, T., Matsuzaki, H., Yamamoto, R., Shiota, N., Okunishi, H., Kihara, M., Umemura, S., Sugiyama, F., Yagami, K., Kasuya, Y., Mochizuki, N., and <u>Fukamizu, A.</u> Regulatory roles for APJ, a seven-transmembrane receptor related to angiotensin-type 1 receptor in blood pressure in vivo. J. Biol. Chem. 279, 26274-26279 (2004)

• Saito, T., Ishida, J., Takimoto-Ohnishi, E., Takamine, S., Shimizu, T., Sugaya, T., Kato, H., Matsuoku, T., Nangaku, M., Kon, Y., Sugiyama, F., Yagami, K., and <u>Fukamizu, A.</u> An essential role for angiotensin II type 1a receptor in pregnancy-associated hypertension with intrauterine growth retardation. FASEB J. 18, 388-390 (2004)

【Term of project】	FY 2005 - 2009	【Budget allocation】	83,300,000 yen
【Homepage address】 http://akif2.tara.tsukuba.ac.jp/			