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Non-Invasive Method for Evaluating Sensitivity to Sodium by Using Mouse Diabetic Kidney Model - Interaction with a Low-Protein Diet

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Summary

Animal experiments are an essential research method for the evaluation of drug efficacy and food functionality in order to examine the effects *in vivo*. In animal experiments, researchers usually performed biochemical analysis, however, this method can only provide limited information at the end of the experiment. In addition, since the same individual animals cannot be analyzed at a tissue level repeatedly, there will be problems with individual differences in pathology and functionality. *In vivo* imaging, which is a non-invasive observation *in vivo*, has become widely used due to the recent development of imaging technology to observe chemiluminescence and fluorescence *in vivo* from outside the body. By *In vivo* imaging, the effects of drugs and functional foods can be evaluated without a large number of experimental animals. We have previously isolated the serum amyloid A3 (Saa3) gene, whose expression is up-regulated upon macrophage infiltration into white adipose tissue, in order to observe chronic inflammation in white adipose tissue non-invasively by *in vivo* imaging. We then generated a transgenic mouse (Saa3-luc mouse), which have a chimeric gene (luciferase gene) linked to the downstream of the promoter of the Saa3 gene and successfully observed chronic inflammation in white adipose tissue non-invasively by *in vivo* imaging.

On the other hand, the number of patients with chronic kidney disease has been increasing in recent years, and functional foods are needed to restore the decreased kidney functions. The aim of this study is to establish a non-invasive method to evaluate the biological response to early diabetic nephropathy and salt intake by observations of the kidney from outside the body based on luciferase activity. To create a diabetic nephropathy model, Saa3-Luc mice were given a high-fat diet and administered with streptozotocin (STZ), followed by a high-fat diet. As another diabetic nephropathy model, after STZ administration, Saa3-Luc mice were given a high-NaCl diet. In both cases, bioluminescence based on Saa3 promoter activity in Saa3-luc mice were promoted in kidney, showing that Saa3 promoter activity is most likely related to diabetic nephropathy. We are currently analyzing kidney bioluminescence of Saa3-luc mice non-invasively and compared with blood markers, and are testing the effect of a feeding of low-protein or high-protein diet with STZ administration.