**Analysis of Nuclear Receptor FXR Controlling Metabolism of Cholesterol**

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Nuclear receptors function as transcription factors that regulate metabolism of glucose, lipid and cholesterol. Dysregulation of these metabolism leads to metabolic syndrome including type 2 diabetes, obesity, dyslipidemia and atherosclerosis. Study of nuclear receptors promises to provide discoveries of therapeutic agents for metabolic syndrome. Nuclear receptors are divided into several domains including the N-terminal A/B domain, the DNA binding domain (C), the hinge region (D) and the C-terminal E/F domain. Nuclear receptors have two regions for transactivation, a constitutive activation function (AF-1) in the A/B domain and a ligand-dependent activation function (AF-2) in the E/F domain. Coactivators required for the AF-2 activity have been well studied, whereas coactivators for the AF-1 activity are poorly understood. To gain insight into AF-1, we isolated proteins associated with AF-1 by GST pull-down assay using the A-C domain of farnesoid X receptor (FXR) and nuclear extract from HeLa cells. Mass spectrometry analysis revealed that DNA-dependent protein kinase (DNA-PK), consisting of Ku70, Ku80 and DNA-PK catalytic subunit (DNA-PKcs), was identified. Next, we examined which domains of FXR are required for the interaction with these factors. As a result, the D-F domain of FXR as well as the A-C domain of FXR was interacted with DNA-PK. We also showed that Ku80 and Ku70 directly interacted with FXR *in vitro* by pull-down assay using bacterially expressed Ku80, Ku70 and FXR. Further, immunoprecipitation assay revealed that DNA-PKcs, Ku80 and Ku70 interacted with FXR *in vivo*. We now attempt to examine an effect of Ku80 and Ku70 on the FXR-mediated promoter activity.