Structural Analysis of PPARα in Complex with Lobeglitazone
Involved in the Anti-diabetic mechanism

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Peroxisome proliferator-activated receptors (PPARs) are ligand-inducible transcription factors that belong to thyroid/retinoid hormone receptor-like nuclear receptors [1,2]. In particular, PPARα as one of the subtype of PPARs is known for regulating the metabolism of fatty acids and lipid homeostasis in various organs [1]. Since PPARα activation has also been found to reduce inflammation, PPARα has been considered to be a potential therapeutic target for cancer as an agonist and antagonist [2-4].

Lobeglitazone is one of TZD(Thiazolidinedione) which is known as an anti-diabetic drug and a recent study revealed lobeglitazone is a dual agonist on PPARα and PPARγ [2, 4]. In clinical use, PPARα has therapeutic effects on dyslipidemia and insulin resistance [3, 4].

As known in previous studies PPARα has a high potency of lobeglitazone as an agonist, however, there was no evidence of a molecular mechanism for lobeglitazone and PPARα complex. Here we report purification steps, PPARα crystals complexed with lobeglitazone, and their X-ray diffraction data. Structural analysis is currently in progress, and it would help elucidate molecular interaction between PPARα and lobeglitazone.