Exploring the Anti-adipogenic Role of YAP/TAZ at the Chromatin Level

Seol, Taejun[1], Kang, Ju-Gyeong[1], Lim, Dae-sik[1]

[1] National Creative Research Center for Cell Plasticity, KAIST Stem Cell Center, Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Daejeon, 34141, Republic of Korea;

Studying adipogenesis—the differentiation of adipocytes from mesenchymal stem cells—is essential for understanding how adipose tissue fulfills its metabolic functions, such as buffering energy flux. Transcriptional coactivator with PDZ-binding motif (TAZ) and its paralog, Yes-associated protein (YAP), are key transcriptional coactivators of the Hippo pathway, playing crucial roles in cell fate determination and tissue development. While TAZ's role in inhibiting adipogenesis has been recognized since the early studies of the Hippo pathway, the underlying mechanisms remain unclear. Here, we demonstrate that YAP and TAZ function as anti-adipogenic factors in adipocytes at the chromatin level, as revealed through high-throughput sequencing analyses. During adipogenesis, Hippo pathway activation suppresses YAP/TAZ activity. Conversely, forced activation of TAZ in C3H10T1/2 differentiation models and mouse white adipose tissue disrupts adipogenesis by reprogramming the adipocyte epigenome and regulating key adipogenic transcription factors. Notably, these functions depend on the transactivation activity of the YAP/TAZ/TEAD complex rather than TAZ's direct interaction with PPARγ, as previously suggested. These findings provide new insights into how the Hippo-YAP/TAZ pathway maintains mesenchymal stem cell stemness at the chromatin level and regulates adipogenesis.