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STUDY ON THE INTERACTION BETWEEN DNA-BINDING DOMAIN (DBD) OF HUMAN ANDROGEN RECEPTOR (AR) AND SWIRM DOMAIN OF LYSINE-SPECIFIC DEMETHYLASE 1 (LSD1)

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Gene regulations of prokaryotes and eukaryotes are different. Prokaryotic gene regulation requires simply binding of regulatory proteins to help with or avoid forming transcription complex. For eukaryotes like humans, however, their regulation needs “chromatin remodeling” with the association of regulatory proteins involving the opening up of DNA-histone protein complex chromatin and unwinding DNA. Without remodeling, RNA polymerases responsible of the transcription process cannot get access and perform transcription.

Lysine-specific demethylase 1 is one of the chromatin remodeling enzymes. It can demethylate specifically the N-tail mono- or di-methylated K4 residue on histone H3 by oxidation (Y. Shi et al., 2004). LSD1 has three known domains: FAD-binding domain, demethylase domain and SWIRM domain. Till now, the exact function of SWIRM domain of LSD1 is still unclear, although its solution structure has been reported.

In 2005, Metzger’s group found that the LSD1 SWIRM domain could bind the N-terminus, the DNA-binding domain (DBD) and the ligand-binding domain (LBD) of androgen receptor (AR) by performing a GST-pull down assay (Metzger et al., 2005); and shows that SWIRM domain has the strongest interaction with DBD among the domains of AR. Therefore, my study is to investigate the interaction between AR-DBD and SWIRM-LSD1 domains by NMR spectroscopy.

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