Targeting estrogen receptors and cofactors for precision medicine in breast cancer

By Xu Wei

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Xu's laboratory focuses on targeting estrogen receptors for breast cancer therapy. Estrogen receptors (ERs) exist in two forms, ERα and ERβ, which have opposing roles in cell proliferation. In a small molecule library screen, Dr. Xu identified a natural plant product Dip G that significantly decreased ERα but increased ERβ stability. Via distinct mechanism from the existing agents for endocrine therapy, this compound also significantly promoted degradation of mutant ERα that is found in ~25% of patients with metastatic ERα-positive breast cancers. Biological functions of these estrogenic compounds are currently being investigated in cell-based and breast cancer mouse models. Dip G may be developed as novel agents for treating metastatic, endocrine-resistant breast cancers caused by ERα mutations.

Dr. Xu’s laboratory has also employed biochemical and functional genomic approaches, as well as mouse genetics to decipher the contribution of histone arginine methylation to the epigenetic control of cancer cells. The major focus of Xu lab is on a protein arginine (R) methyltransferase CARM1/PRMT4, a nuclear hormone receptor co-activator. Using genetically engineered CARM1 knockout cell lines, Dr. Xu has identified a number of non-histone substrates for CARM1 and elucidated the function of protein arginine methylation in cancer initiation, progression and metastasis.