**To build and visualize chromatin: Understanding epigenetic memory**

Minhee Park

KAIST, Department of Biological Sciences

Epigenetics compose a powerful layer of regulation, credited with the classical example of establishing and perpetuating gene expression patterns that enable cells with identical genomes to exhibit distinct phenotypes. This power inspires repurposing epigenetic elements for the development of next-generation cellular molecular therapies. However, defining *sufficiency* for integral properties such as durable inheritance responses has remained elusive due to technical limitations and the lack of experimental platforms.

We apply a bottom-up synthetic biology approach to develop a minimal synthetic epigenetic system based on the principle of classic “read-write” motif to evaluate epigenetic memory. We exploit DNA adenine methylation (6mA), a DNA modification that is rarely found in metazoan genomes, to create a fully synthetic chromatin system in human cells. Together with a quantitative model of chromatin dynamics, we show these circuits mediate spreading of the modification to regulate genes at a distance and the establishment of long-term epigenetic memory, demonstrating the sufficiency of the read-write mechanism for epigenetic memory.

We also explore additional mechanisms (or “motifs”) governing epigenetic regulation, one of which is the 3D chromatin structure. We combine user-defined synthetic control of epigenetic silencing and super-resolution 3D chromatin imaging to systematically and quantitatively delineate 3D chromatin organization and epigenetic memory mechanisms at single-nucleus resolution.