Uncovering a reversible master switch for development

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In a paper published in *Genes & Development*, BWH principal investigator Mitzi Kuroda, PhD, and her team identified a reversible "master switch" on most developmental genes. The team unearthed this biological insight through studies in the fruit fly —a powerful model organism for studying how human genes are organized and function.

The human genome contains billions of DNA "letters," that can only be read as words, phrases and sentences with the help of proteins that, metaphorically, mark the DNA with punctuation. Together, the DNA-protein combinations form chromatin which provides the essential annotation for gene transcription. However, it is still not understood how the annotation and readout of a single genome differs across cell types. The differences are crucial for normal development and are mutated in cancer. Currently, it is thought that different combinations of proteins act at each of the thousands of genes, and deciphering the numerous complex patterns is a difficult task.

In Kang et al., the Kuroda lab identifies a reversible "master switch" that sits on potentially all developmental genes in a model organism, the fruit fly. Their bivalent master switch model provides a conceptually simple explanation for how each developmental step is made along the path to different cell types, dependent on cell type-specific proteins, but acting through this common module.

In this case the fly model is likely to extend and synergize with seminal work by Harvard Medical School professor Brad Bernstein, MD, PhD, and colleagues on the regulation of key developmental genes in mammalian embryos.

More information: Hyuckjoon Kang et al, Bivalent complexes of PRC1 with orthologs of BRD4 and MOZ/MORF target developmental genes in Drosophila, *Genes & Development* (2017). DOI: 10.1101/gad.305987.117

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