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Decoding the regulatory architecture in Drosophila Hox gene enhancers

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In *Drosophila*, the Abdominal-B homeotic (Hox) gene is expressed in a spatially and temporally restricted pattern along the anterior-posterior axis during embryonic development. The transcription pattern is controlled through specific interactions between transcription factors and a number of enhancers in the neighboring intergenic region. Using computational, mathematical modeling and experimental molecular genetic approaches we investigate how the architecture of transcription factor binding sites mediates the functional activity of these enhancers. A cross-species comparison of the enhancers reveals an evolutionarily conserved signature motif containing two FUSHI-TARAZU activator binding sites that appear to be acting in a cooperative manner. We also find that the transcriptional repressors KNIRPS, KRUPPEL and GIANT are able to restrict gene expression from the enhancers through different molecular mechanisms including short-range repression and competitive binding. Thermodynamic mathematical models can accurately predict the regulatory logic at the enhancers. Our results demonstrate that the transcriptional output of the enhancers relies on a complex set of combinatorial inputs mediated by specific transcription factor binding sites and that the sequence architecture at the enhancers is critical to maintain robust regulatory function.

Biography

Robert A Drewell completed his PhD at Cambridge University in 1999 and conducted Postdoctoral studies at University of California, Berkeley and California Institute of Technology. He is an Associate Professor at Clark University and has published more than 30 papers.

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