Department of Biology
The College of Arts + Sciences | Indiana University Bloomington

Distinguished Alumni Award Lecture

[Day/Date], 2021 • [Time] • Myers Hall 130

James Birchler, Ph.D.

Curators' Professor of Biological Sciences, University of Missouri

The Gene Balance Hypothesis

How regulatory gene stoichiometries affect expression, the phenotype, and evolutionary processes

Changes in chromosomal dosage were found to modulate gene expression in maize at IU. A dosage series of the long arm of chromosome 1 produced primarily an inverse correlation of selected gene expression across the genome. Experiments in *Drosophila* showed similar results. Single genes—primarily transcription factors, signal transduction components, and chromatin proteins—were identified that produced dosage effects on target genes. RNA-seq experiments in *Drosophila* and *Arabidopsis* indicated that global trans effects of trisomy can be varied but the most common deviation from normal is a reduced expression more or less within the inverse range (down to 0.67), although outlying peaks were also found that extend positively and negatively. Recent global studies of gene expression in a large set of aneuploids including monosomies, trisomies, tetrasomies, and disomic haploids as well as multiple ploidy levels in maize revealed the spectrum of extensive modulations. Whole genome dosage changes (polyploidy) showed many fewer relative modulations suggesting a stoichiometric or balance component to gene regulation. Re-analysis of studies of gene expression in disomic haploids of yeast and trisomics of mice revealed the topology of gene expression modulations with the most common effect being a reduced expression in trans by hyperploidy. The dosage sensitivity of regulatory mechanisms and the control of quantitative traits are similar suggesting a connection. The studies in maize, *Drosophila*, and *Arabidopsis* indicate a connection between dosage compensation of the varied genes on aneuploid chromosomes and the trans-acting inverse effect, which has implications for the evolution of sex chromosomes. Duplicate genes have different evolutionary fates depending on the mode of duplication (i.e., the whole genome or segmental regions). The stoichiometric effects are postulated to explain this trend. The recognition of similar aneuploidy effects in monocots, dicots, fungi, insects, and mammals and their connection with dosage compensation suggests that these effects are a general reflection of an imbalance of regulatory gene products in the processes of gene expression.

Hosted by the faculty of the Department of Biology
Refreshments served prior to lecture; reception held immediately after seminar

About James Birchler

James "Jim" Birchler started "playing around with the chromosome arms of maize" while studying genetics in Drew Schwartz's lab at Indiana University, from where he received his Ph.D. in 1977. He did his postdoctoral fellowship studying gene dosage mechanisms in fruit flies at Oak Ridge National Laboratory and the University of California, Berkeley. He served on the Harvard University faculty from 1985 until he joined the faculty at the University of Missouri in 1991. Birchler was elected to the National Academy of Sciences in 2011.

He is known by the fly world as the scientist who discovered cosuppression in *Drosophila* and by the plant world as the cytogeneticist who figured out how to paint, break, and regrow plant chromosomes. He's also known for his impressive ability to engage his students. Birchler coined the term "chromosomeomics," and developed a fast-flowering mini maize that, according to *The Plant Cell*, is "poised to beat *Arabidopsis* in a seed-to-seed race."

Support for this lecture was provided by the IU Department of Biology and the IU College of Arts and Sciences Office of Advancement.