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Thomas W. Cline

The 2010 Novitski Prize: Thomas W. Cline

IT is a pleasure to recognize Thomas W. Cline as the recipient of the Novitski Prize for 2010. The award, named in honor of Drosophila geneticist Edward Novitski (1918–2006) and supported through the generosity of his family, was established to recognize an exceptional level of creativity and intellectual ingenuity in solving significant problems in biology through the application of genetic methods. This award specifically recognizes Tom's early genetic studies that establish *Sex-lethal* (*Sxl*) as the binary switch gene that controls Drosophila sex determination and dosage compensation.

By Tom's own account (see Perspectives article by Cline 2005), his work on sex determination began by chance when he happened upon a description of the *daughterless* (*da*) mutant phenotype (Cline 1976). Serendipity also played a role in initiating a chain of experiments that led to his discovery that the maternally provided *da* gene product is needed to relay X chromosome number to *Sxl* (Cline 1978, 1979, 1980, 1983). The story begins with the discovery of a spontaneous X-linked male-lethal mutation that allows female embryos to survive the female-lethal *da* maternal effect. Through mapping, and the creation of double mutants, Tom formally proved that this male-lethal mutation (Sxl^{M1}) was a gain-of-function allele of the previously identified X-linked female-lethal mutation (Sxl^{f1}). It was, however, the exhaustive analysis of these loss- and gain- of- function sex-specific lethal phenotypes that led to the unanticipated but inescapable conclusion that sex and death are connected, as *Sxl* was discovered to be required for both promoting the female differentiation pathway and silencing the male dosage compensation system.

In 1984, in a masterful tour-de-force genetic study, Tom made the remarkable discovery that *Sxl* autoregulates (Cline 1984). Tom's earlier studies had already shown that *Sxl* activity is needed throughout development even though the *da*-mediated X-chromosome dose signal required to trigger its activation was limited to early embryogenesis. The data in this article, generated from a dizzying array of genetic crosses with unusual double- mutant *Sxl* alleles, lead to the unequivocal conclusion that in the absence of the normal *da*-mediated activating mechanism, some mutant alleles were able to activate Sxl^{+} alleles in *trans*. What is notable about this body of work is the unerring logic that led Tom to propose that *Sxl* converts the transient X chromosome- driven sex-fate decision into long- term cellular memory by positively regulating its own expression. This prophetic model, now fully vindicated by molecular data (Bell *et al.* 1991), is a sterling testament to the power of genetics.

Over the course of his career, Tom has continued to use ingenious genetic approaches in his quest to discover the components and mechanisms cells use to determine their sexual fate. Tom's continuous application of logic, elegance, and artistry to his experimental approaches makes him an especially deserving candidate for this year's Novitski Prize.

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