

Spatio-temporal regulatory landscape of sex-determination

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http://marciuslab.org
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Sex determination: a 3,000 year-old enigma

Mythology



Hermaphrodite primeval men Plato's symposium, 385-370 BC

Theories



Left-right theory Alexandrian manuscripts, 1st cent. BC Genetics



Discovery of Sry gene Koopman et al., Nature, 1991 (Goodfellow & Lovell Badge labs)

Hi-C & ChIP-seq



Dekker, J., Rippe, K., Dekker, M., & Kleckner, N. (2002). Science, 295(5558), 1306–1311. Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293.





Sex-determination as a model for "bipotential" commitment



No major structural (apparent) differences







Hi-C normalization and interaction selection

chr11:110780000-114770000















Local Moran Index











All genes LMI Trip

36

Log10(pval)

--6

136

28

266

Log10(pval)



20





Now that we know the genes.... Can we identify regulatory elements using

Fgf9 locus chr14:56,070,000-60,070,000







Chromosome 14

Fgf9 locus chr14:56,070,000-60,070,000



Fgf9 XY Δ 306 mutant



Fgf9 XY Δ 306 mutant

XY Wildtype

XY Δ306

XX Wildtype



0/16



Fgf9 XY Δ 306 mutant



Fgf9 XY additional mutants



Take home messages:

First characterization of the 3D regulatory landscape of sex determination

METALoci is an unbiased approach to quantify gene regulatory activity

METALoci is a predictive tool to identify critical regulatory loci

Discovery of a novel non-coding region controlling sex determination

Take home messages:











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In collaboration with the Capel Lab (Duke U.) and Lupiañez Lab (MDC Berlin)

.: Our current sponsors :.













.: Conflict of Interest Statement :.

Marc A. Marti-Renom serves as a consultant to Acuity Spatial Genomics, Inc., and receives compensation for these services.