A MALE-SPECIFIC microRNA IS ESSENTIAL FOR AVIAN SEX CHROMOSOME DOSAGE COMPENSATION

Fallahshahroudi et al. (1) have uncovered a unique sex chromosome dosage compensation mechanism in birds, where male-essential microRNA (miR-2954) plays a critical role in male survival. Avian sex determination differs from mammals, with females being heterogametic (ZW) and males homogametic (ZZ). The W chromosome has undergone significant gene loss during evolution, raising questions about how birds balance gene dosage between sexes. This study reveals that miR-2954, which exhibits strong male-biased expression, counteracts the effects of transcriptional and translational upregulation of dosage-sensitive Z-linked genes.

The authors used CRISPR-Cas9 technology to knock out miR-2954 in chickens, leading to early embryonic lethality in homozygous knockout males. This lethality is likely caused by the specific upregulation of dosage-sensitive Z-linked target genes. Evolutionary gene expression analyses further demonstrated that these target genes underwent both transcriptional and translational upregulation on the single Z chromosome in females. The findings suggest that evolutionary pressures following W gene loss drove the upregulation of dosage-sensitive Z-linked genes in both sexes, with miR-2954 emerging to offset the resulting excess of transcripts in males. This study provides insights into the complex interplay between gene dosage, sex chromosome evolution, and the emergence of regulatory mechanisms in birds.

1. https://doi.org/10.1038/s41586-025-09256-9