

SEX CHROMOSOME GENE DOSAGE INFLUENCES CARDIOMETABOLIC HEALTH AND DISEASE

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Many aspects of metabolism are sex-biased, from gene expression in metabolic tissues to the prevalence and pathology of cardiometabolic diseases. The influence of hormones produced by male and female gonads has been widely documented, but recent studies have begun to elucidate the impact of genetic sex (XX or XY chromosomes) on cellular and organismal metabolism. XX and XY cells have differential gene dosage conferred by specific genes that escape X chromosome inactivation or the presence of Y chromosome genes that are absent from XX cells. Studies in mouse models that dissociate chromosomal and gonadal sex have uncovered mechanisms by which chromosomal sex influences diseases such as obesity, atherosclerosis, pulmonary hypertension, autoimmune disease, and Alzheimer's disease. I will illustrate the influence of sex chromosome complement and specific genes on the X chromosome in the development of obesity and related cardiometabolic conditions. These studies identify genetic and epigenetic mechanisms underlying sex differences in health and disease.