GENETICS

X ACTIVITY CENTER

males are therefore most likely X mosaics.

6.02.2008 1 COMMENT

A recent editorial in PLoS Biology was about "Sex, dose and equality". I always had problems to understand X linked recessive disease and carrier status of a woman: If the random X inactivation would have been complete why are there not much more colorblind women? Obviously the second X is at least partially active as a rescue system. The mechanisms of X inactivation seems to be extremely complicated: With the appearance of the Y chromosome, the Xist locus is being methylated; otherwise the unmethylated Xist locus is leading to RNA expression and inactivation of the second X. This is not a stable process as it needs *eed* also on the X chromosome which itself reactivates Xist. Fe-

This is acknowledged at the end of the "Sex, dose and equality":

There is a large body of literature on the mechanism of X inactivation, which involves the expression of a noncoding RNA (Xist) from the X inactivation center, some type of cis-recognition of the chromosome to inactivate, chromatin modification, and condensation ... that the gradual inactivation occurs in groups of genes by spreading into the X-chromosome territory. The idea that mosaic inactivation is dependent on the proximity to the Xist locus in three-dimensional chromosome-territory space is attractive...

I propose to do an experiment similiar to one that I found <u>last year in Science</u>. Allele specific expression

uses a rather simple principle where the allelic ratio of a heterocygous SNP within a RNA transcript is taken as a measure of gene expression from the different chromosomes (that are carrying either the one or the other SNP allele).

Given that there are enough informative SNPs in every X gene, mosaic expression status should be easy to examine (the PLoS editorial even cited some interesting X expression studies that I was not aware of — ref 12-15). Reading the editorial a second time, I even disagree with the main hypothesis that

This wild-type alteration is therefore a very powerful model for understanding how networks respond to gene dose.

I believe that the XY system represents a very special situation that does not compare to general gene dosage analysis. The suggested approach of single gene expression analysis seems to be adequate. Taken the arguments in the editorial to an extreme, where a single X is required to produce the same amout of RNA as two autosomes, I would even expect a X activity center, Xact;-)

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admin

23.02.2008 AT 10:05

Ref also believes that inactivation is not random.

Ref has many clinical examples for skewing in the introduction.

Ref shows skewing is often observed in tumor clonality.

Ref believes in a stochastic process of X inactivation but also a X activity center.

Ref confirms the generally accepted 2fold upregulation of X genes.

COMMENTS ARE CLOSED.