## Protection from X inactivation

SIR — Davies in News and Views<sup>1</sup> draws attention to the growing literature on genes on the X chromosome that are not subject to inactivation, and to the now established finding that such genes are not confined to a single contiguous region extending from the telomere of the short arm. This distribution cannot be accounted for by arrest of a spreading inactivation process. The finding that this class of genes includes some that are also present (although with minor sequence differences) on the Y chromosome suggests a possible solution to the problem of the mechanism of local and distributed protection from inactivation.

A widely accepted explanation<sup>2</sup> for inactivation of one X chromosome is that inactivation ensures that the dosage of genes is the same in the female (with an XX complement) as in the male (who with an XY complement carries only one copy of X-linked genes). A similar dosage problem can be seen to exist for any Y-linked genes not involved in sex determination. Such genes may be presumed to have an active homologue on the X-chromosome, and to maintain dosage equilibrium they would be expected not to be subject to inactivation in the female.

How could such protection of X-Y-homologous genes linked achieved? A possible answer is that they might be protected by sequence specific pairing in male meiosis from a process of genomic imprinting. Pairing of X and Y chromosomes in male meiosis is known to extend well beyond the 'pseudoautosomal region' within which there is strict sequence homology and recombination between X and Y (ref. 3). Genes outside this region present only on the X chromosome would be subject to imprinting, whereas those with homologous (although perhaps not identical) sequences on the Y chromosome would be protected.

The hypothesis predicts the following: (1) protection from inactivation will occur when the X chromosome that is preferentially inactivated in the female is the unpaired paternal X. In marsupials and for trophectoderm and primitive endoderm (but not for primitive ectoderm and its embryonic derivatives $^{4,5}$ ) in the mouse it is the paternal X that is consistently inactivated. However in primitive ectoderm in the mouse, and in man, which X chromosome is inactivated is apparently random. A test of the hypothesis therefore is whether X-Y homologous genes remain active on an inactivated X chromosome that is maternal in origin. (2) Pairing of X-Y homologous genes (for example, ZFY and RPS4Y in Yp11.3 with ZFX in Xp21 (ref. 6) and RPS4X in Xq13 (ref. 7),

respectively) requires an unusual configuration in male meiosis. If such a configuration occurs it might be detected by electron microscopic examination of surface spread synaptonemal complexes.

According to this hypothesis genes on the Y chromosome (other than those that determine sex) are predicted in each case to have a homologue on the X chromosome that is not subject to inactivation. Conversely, genes that are not inactivated on the X chromosome will be expected to have a homologue on the Y. An apparent exception to this rule is A1S9T, a gene that lacks a Y homologue and had been thought<sup>8</sup> to escape inactivation. It now seems, however, that this gene is susceptible to the normal inactivation process<sup>9</sup>. Therefore, the principle that X-linked genes that escape inactivation are also represented on the Y chromosome is preserved, and X-Y pairing in male meiosis deserves consideration as a possible mechanism.

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## Chitin and nodulation

SIR - In the yeast Saccharomyces cerevisiae, the CSD2 gene is required for chitin synthase III activity and for synthesis of 90% of the cellular chitin<sup>1</sup>. A FASTA search of the TRANSGEN protein database using the deduced aminoacid sequence of CSD2 reveals significant similarities to chitin synthases, as expected, to *nodC* proteins from several

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(poly-N-acetyl- $\beta$ -1,4-D-glucosamine), together with the similarity between the nodC and CSD2 gene products, suggest that nodC encodes an N-acetylglucosaminyltransferase that synthesizes oligosaccharide backbone NodRm-1. The similarity of the nodC protein to DG42, a gastrulation-specific protein<sup>3</sup>, is noteworthy (FASTA \* · · · · \* · · \* · · ·

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SVDYVO-VCD SDTKLDELAT VEMVKVLESN DMYGAVGGDV RILNPYDSF- ----ISFMSS
DG42
      SGDLVL-NVD SDSTIAFDVV SKL-ASKMRD PEVGAVMGQL TASNSGDTW- ----LTKLID
nodC
      FYETVL-MVD ADTKVFPDAL THMVAEMVKD PLIMGLCGET KIANKAQSW- ----VTAIQV
CSD2
CHS2
      LQPTVVTLVD VGTRLNNTAI YRLWKVFDMD SNVAGAAGQI KTMKGKWGLK LFNPLVASQN
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LRYWMAFNVE RACQSYFDCV SCISGPLGMY RNN----- ----ILQV FLEAWYRQKF DG42 nodC MEYWLACNEE RAAOSRFGAV MCCCGPCAMY RRS----- ----ALAS LLDQYETQLF FEYYISHHOA KAFESVFGSV TCLPGCFSMY RIKSPKGSDG YWVPVLANPD IVERYSDNVT CSD2 FEYKISNILD KPLESVFGYI SVLPGALSAY RYRALKNHED GTGPL--RSY FLGETQEGRD CHS2

LGTYCT---- LGDDRHLTNR -VLS--MGYR TKYTHKSRAF SETPSLYLRW LNQQTRWTKS DG42 RGKPSD---- FGEDRHLTI- LMLK--AGFR TEYVPDAIVA TVVPDTLKPY LRQQLRWARS nodC NTLHKKNLLL LGEDRFLSS- LMLKTFPKRK QVFVPKAACK TIAPDKFKVL LSQRRRWINS CHS2 HDVFTAN-MY LAEDRILCWE LVAKRDAKWV LKYVKEATGE TDVPEDVSEF ISQRRRWLNG

Alignment of the sequences of the CHS2, CSD2 (GenBank accession number M73697) nodC and DG42 proteins. The region displayed exhibits 30% identity between CHS2 and CSD2 (11.5 s.d. above random), 32% identity between CSD2 and nodC (6.0 s.d. above random), and 25% identity between CSD2 and DG42 (8.2 s.d. above random). The program BESTFIT was used. The marks above the sequences indicate the number of identical amino acids: a dot indicates two, an asterisk three, and a bold asterisk four.

of Rhizobium bacteria  $(initn=280 \text{ for } R. \text{ } meliloti^2), \text{ and to the}$ DG42 protein of the amphibian Xenopus laevis<sup>3</sup> (initn=173). DIAGON comparisons of each of these proteins to the CSD2 protein identify a common region of  $\sim$ 180 amino acids.

The functions of the nodC and DG42 proteins are unknown: nodC is required for nodulation in all species of Rhizobium<sup>4</sup> and for synthesis of the extracellular nodulation factor, NodRm-1, a sulphated N-acyl-tri-N-acetyl- $\beta$ -1,4-D-glucosamine tetrasaccharide<sup>5</sup>. relationship of this molecule to chitin initn=342). Could oligosaccharides like NodRm-1 serve as signals during embryogenesis?

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