The degenerate Y chromosome – can conversion save it?

Jennifer A. Marshall Graves

Research School of Biological Sciences, The Australian National University, Canberra, ACT, Australia. email: jenny.graves@anu.edu.au

Abstract. The human Y chromosome is running out of time. In the last 300 million years, it has lost 1393 of its original 1438 genes, and at this rate it will lose the last 45 in a mere 10 million years. But there has been a proposal that perhaps rescue is at hand in the form of recently discovered gene conversion within palindromes. However, I argue here that although conversion will increase the frequency of variation of the Y (particularly amplification) between Y chromosomes in a population, it will not lead to a drive towards a more functional Y. The forces of evolution have made the Y a genetically isolated, non-recombining entity, vulnerable to genetic drift and selection for favourable new variants sharing the Y with damaging mutations. Perhaps it will even speed up the decline of the Y chromosome and the onset of a new round of sex-chromosome differentiation. The struggle to preserve males may perhaps lead to hominid speciation.

The human Y chromosome

In human beings, as in other mammals, sex is determined by a heteromorphic pair of sex chromosomes. The X is large and bears many genes, whereas the Y is small and heterochromatic and almost devoid of active genes. Normally, an XX chromosome constitution specifies female development and XY, male development.

Human sex chromosomes are typical for eutherian (‘placental’) mammals. Figure 1 shows the structure and gene content of human sex chromosomes. The X is a middle-sized chromosome (165 megabases (Mb)) with 1438 genes at the last count, most of which have nothing to do with sex (http://www.gdb.org/hugo/chrX/geneSummary.html accessed April 2004). The Y is much smaller (67 Mb), and seems to be largely composed of repetitive sequences that give it a heterochromatic appearance. Although repetitive sequences are not necessarily junk, ~40 Mb on the long arm of the Y comprise two simple repeats. The 25 Mb of ‘euchromatic’ Y chromosome are also very rich in repetitive sequences. The two extremities of the Y chromosome are homologous with the termini of the X chromosome and pair with them at male meiosis. These ‘pseudoautosomal regions’ (PARs) recombine just like ordinary autosomes. Outside this region, the male-specific region of the Y chromosome (MSY) does not recombine with the X. Therein lies its problem, because non-recombining parts of the genome tend to decay rapidly.

Genes on the Y chromosome

The number of genes on the human Y have been counted and recounted, and the significance of the gene content for function and evolution has been debated for decades. Now we have the full sequence of the Y chromosome (Skaletsky et al. 2003), numbers are no longer controversial; however, the significance of the Y chromosome is likely to be even more vigorously debated.

Other than sex determination, few traits could initially be ascribed to the Y, and gene discovery by deletion analysis was slow and difficult. We have known for 45 years that people with a Y chromosome are male, no matter how many X chromosomes they have (Ford et al. 1959; Jacobs and Strong 1959). After a long search, it was discovered that the Y bears a male-dominant gene, SRY, that switches on testis differentiation in the embryo (Sinclair et al. 1990), which then churns out powerful masculinising hormones. Thus, the most dramatic phenotypic difference between people is caused by a single gene.

Several other genes on the Y chromosome have functions in spermatogenesis, as evidenced by the effects of deletions, and they are expressed only in the testis (Reijo et al. 1995). This led Lahn and Page (1997) to propose that the male-specific region of the Y was ‘functionally coherent’ in a way that no other chromosome is. However, the Y contains some genes that seem to have nothing to do with being male; for instance, one codes for tooth enamel and another for a ribosomal protein (summarised by Skaletsky et al. 2003).

Even the complete sequencing of the human genome (Lander et al. 2001) did not solve the problem of the Y. Its repetitive sequence content made it impossible to line up large insert clones, let alone small shotgun fragments, by detecting overlapping sequences that might be represented at many different sites. However, complete sequencing of the male-specific region has finally been accomplished: a heroic effort led by David Page’s group at the Whitehead Institute in Boston, MA, USA (Skaletsky et al. 2003). Thus, we now have a nearly complete inventory of genes, pseudogenes and transcribed units on the Y chromosome.
This immense sequencing effort has netted a grand total of 27 different protein-coding genes within the 23-Mb male-specific euchromatic region of the Y (Fig. 1). The number of protein-coding genes is swollen to 158 by the presence of many of them in multiple copies and the inclusion of many transcription units that do not code for protein. In addition, there are 18 active genes crowded into the two tiny PARs (totaling 3 Mb) at each end of the Y.

There have been arguments for years as to whether the Y can be fairly described as a ‘genetic wasteland’ (Graves 2000, 2002), or whether the Y has a gene content comparable to other chromosomes (Lahn and Page 1999a; Skaletsky et al. 2003). However, wasteland or no, it is hard to ignore the discrepancy between the density of active genes on the Y (1/2 a gene per Mb) compared to that on the X (~10 genes per Mb).

The peculiarities of the Y chromosome may make no functional sense, but are easily explained by its evolutionary history.

**Evolution of the Y chromosome**

The X and Y chromosome are strikingly different in size and gene content, but there is good evidence to support the hypothesis that they differentiated from an ordinary autosomal pair in an ancient mammalian ancestor.

The mammal XY pair is not shared by other vertebrates. For instance, birds and snakes have a ZZ male : ZW female system that has no homology with the XY pair (Nanda et al. 1999; Graves and Shetty 2001), and many reptiles do not have sex chromosomes at all, relying on temperature differences during incubation to pull the male-determining trigger. The original chromosomes that formed the XY and ZW pairs may still be seen in marine turtles, which have karyotypes almost identical to those of chicken, but possess no sex chromosomes. The chicken Z is represented in the turtle by autosome 5, and the mammal XY by parts of turtle (and chicken) chromosomes 4 and 1 (Graves and Shetty 2001). Birds and reptiles lack an SRY gene; instead, differential dosage of a Z-borne gene DMRT1 may determine sex (Raymond et al. 1998).

The hypothesis that sex chromosomes differentiated from an ancestral autosomal pair was put forward to explain the heteromorphic sex chromosomes of different snake families (Ohno 1967), but applies equally well to humans and other mammals. When one member of this pair acquired a sex-determining allele, this predisposed it to accumulate other alleles advantageous in that sex and neutral or even disadvantageous in the other (Rice 1987). For instance, it has been suggested that variants conferring an advantage in males (e.g. spermatogenesis) accumulated around a male-determining locus on a proto-Y chromosome. Once this clustering occurred, it became advantageous to keep the male-specific gene package together, so recombination between the proto-X and proto-Y became reduced (Charlesworth 1991).

Suppression of recombination is detrimental to any chromosome region. Once a region is genetically isolated, it can no longer repair itself by piecing together the good bits of two damaged chromosomes. In the Y chromosome, the non-recombining MSY region therefore undergoes mutation, deletion, insertion of retroelements and amplification of repetitive sequences (Charlesworth 1991). It rapidly degrades, losing active genes.

It might be expected that selection would preserve the Y chromosome in its pristine state. However, selection does not work very well on the Y. There are several possible reasons for this, including genetic drift and genetic hitchhiking, on top of a high rate of variation. The Y chromosome is particularly vulnerable to mutation. Comparisons of the frequency of synonymous and non-synonymous nucleotide substitutions in Y genes and their X-borne partners in primates and mice shows that in each case, the Y-borne copy is much more rapidly mutated (Wyckoff et al. 2002). This may be because it, alone in the genome, is always passed from generation to generation through the testis. This appears to be a hazardous place for a chromosome to be and it is now clear that most de novo mutations in humans are derived from the male parent (Makova and Li 2002). Spermatogonia must undergo many more division cycles in the testis than do oogonia in the ovary, so the chances of an error occurring at replication are far higher (Miyata et al. 1987). In addition, the sperm is a hostile environment for a gene, being a ‘hotbed’ of oxidation, and devoid of repair enzymes (Aitken and Graves 2002). For this reason, most new human mutations turn out to have come from the male parent. The generation of this variation speeds up the loss of functional genes from the Y by genetic drift and hitchhiking.

In the absence of recombination, the Y is at the mercy of genetic drift, which acts in the Y chromosome in a ratchet-like way (Charlesworth 1991). This is a particularly strong force in small populations and is exacerbated by the 4-fold lower frequency of Y chromosomes in the population (half the population have no Y and the other half have only one, whereas the autosomes are all present in duplicate in every person). If, in a population of Y chromosomes that cannot recombine with each other, the class of Y chromosomes with no damage is accidentally lost because its bearers have no sons, this ‘zero-hit’ class can never be regained. Once lost, they are gone forever – Muller’s ratchet has turned once. Subsequently, the class with one hit may be randomly lost, then the 2-hit class, and so on.

A second powerful force driving the Y to degrade is genetic hitchhiking. This occurs when a new allele with a major effect on male fitness arises on a particular Y chromosome. It sweeps through the population, regardless of what other damaged genes are carried on the same Y (Rice 1987). These two mechanisms can nullify selection for undamaged Y chromosomes that carry a full complement of functional genes.

Variation, drift and hitchhiking have all taken place independently in different mammal lineages, giving rise to loss of different subsets of genes from the Y of, for instance, human beings, mice and dogs. This gives the Y its uniquely
variable gene content between mammal species. Some genes have disappeared from the Y in one lineage but not another. For instance, the UBE1 gene, which codes for a ubiquitin-activating enzyme, has a Y-borne as well as an X-borne copy in mice and marsupials, but not in human beings (Graves 2002). Conversely, the RPS4 gene, which codes for a ribosomal subunit, has copies on the X and Y chromosome in human beings, but has lost its Y homologue in mice (reviewed by Graves 1995). The sex-reversing gene ATRX has a testis-specific Y-borne homologue in marsupials, but this has been lost in all eutherian mammals (Pask et al. 2000).

Attrition of the Y chromosome seems to have occurred in stages, reflected by ‘geological layers’ of the X that are still apparent in the relationship of X genes to their partners on the Y. This suggests that the Y chromosome has undergone a few major rearrangements that destroyed pairing and recombination with the X over a considerable region (Lahn and Page 1999b; Skaletsky et al. 2003). Though the literal use of $K_a/K_S$ ratios has been criticised and the boundaries of the layers have been challenged (Sandstedt and Tucker 2004), there is independent evidence that different parts of the Y have independent origins.

The major geological divide that distinguishes regions of the eutherian sex chromosomes resulted from addition of an autosomal region to both the X and Y ~100 million years ago (Graves 1995). Comparative gene mapping shows that part of the human X (the long arm and pericentric region) is present on the X in all mammals, whereas part is autosomal in marsupials and monotremes (reviewed by Graves 1995). This implies that the eutherian X evolved from at least two different genome regions. The X-conserved region reflects an ancient X present in the common ancestor of all mammals and is represented by chicken chromosome 4. The rest was added more recently in eutherian mammals only and is equivalent to part of chicken chromosome 1 (Graves and Shetty 2001).

The human Y chromosome, too, is composed of a corresponding conserved region, whose genes are present also on the Y in marsupials, and a recently added region, whose genes are autosomal in marsupials. Surprisingly, nearly the entire human Y chromosome is derived from the recently added region (Waters et al. 2001). Only four genes (including SRY) within ~10 Mb were on the original mammalian Y chromosome.

Thus, the paucity of genes on the Y chromosome, as well as the Y’s variability between species, reflects the unique selective forces acting on the Y.

**Evolution of Y-chromosome-borne genes**

The hypothesis that the X and Y differentiated from an autosomal pair as the Y degraded (Ohno 1967; Charlesworth 1991) predicts that genes on the Y evolved from ancestral genes that are still represented on the X. In line with this expectation, most genes and many pseudogenes on the Y have X-borne homologues, from which they obviously evolved.

However, Lahn and Page (1997) suggested that all the interesting, male-specific genes on the Y were acquired, instead, from autosomes. This ‘selfish Y hypothesis’ (Hurst 1994) seems to account for two testis-specific genes that have no X-homologues (Lahn and Page 1999a). DAZ is homologous to a gene DAZL, which appears to have spawned a copy on the Y, which has since been amplified into four copies (Reijo et al. 1995; Repping et al. 2003b). CDY lacks introns and seems to have been derived from a retrotransposed gene copy (Lahn and Page 1999a).

Inconsistent with this hypothesis are the observations that at least four genes with a known male-specific function have homologues on the X from which they clearly evolved. For instance, the multi-copy spermatogenesis gene RBMY evolved from a ubiquitously expressed partner RBMX on the X (Delbridge et al. 1999; Mazeyrat et al. 1999), as did the testis-specific TSPY from a ubiquitously expressed TSPX (Delbridge et al. in press) and USP9Y, shown to be required for spermatogenesis in human beings (Sun et al. 1999), and Ube1y in mice (reviewed by Graves 2002). Even SRY itself evolved from a widely expressed gene SOX3 on the X (Foster and Graves 1994). Several genes show different degrees of inactivity, amplification and male specificity in different species. For instance, ZFY has a ubiquitously expressed homologue on the X (ZFX) in all mammals. ZFY is single copy and ubiquitous in human beings, but is duplicated and testis-specific in mice (reviewed by Graves 2002). It is amplified manyfold in some wild mouse species (Nagamine 1994). Thus, the distinction between single-copy genes with X homologues and multi-copy testis-specific genes is probably meaningless, reflecting evolutionary events after location on the Y, rather than their evolutionary origin.

How did the Y chromosome become so specialised for male function and retain so few genes? The process by which genes became inactivated and lost, or acquired a male-specific function, has been examined by comparing genes at different stages of degradation within different evolutionary layers of the Y chromosome (Graves 2002). The PAR contains active genes that are still paired by the Y, and represent a last hold-out against Y degradation. Genes within the male-specific region show a spectrum of activity, from fully active and ubiquitous, through partially active to inactive pseudogene. Several genes have acquired a male-specific function. Most of these appear to be relics of genes on the original autosome. They may have acquired a selectable function (as has Zfy in mice), or they may be retained simply because they are part of a recent inversion and have not yet had time to get lost (the tooth enamel gene AMELY, which is represented only by a pseudogene on the mouse Y, may be an example). Within the conserved ancient region of the human Y, only four relics of original genes survive, including SRY and RBMY. The overwhelming majority of genes have been completely deleted from this region of the Y (Waters et al. 2001; reviewed by Graves 2002).
Different stages of degradation and loss may also be shown by the same gene in different species. For instance, *UBE1Y* is pseudoautosomal in monotremes, active but male-specific in mice and marsupials, present only as pseudogene fragments in several primates and has been completely lost from the human Y (Mitchell *et al*. 1998).

Amplification is also a frequent occurrence on the Y chromosome, and occurs in genes on the added region as well as the ancient conserved region. For instance, the candidate spermatogenesis gene, *RBMY*, was shaped by internal exon amplification (Delbridge *et al*. 1999), and has also been amplified independently in several eutherian and marsupial lineages (Delbridge *et al*. 1997). *Zfy* and even *Sry* have been amplified in some old world mice (Mitchell *et al*. 1998). It is likely that amplification of genes on the Y is selected for to compensate for the decrease of activity following a mutation (Graves *et al*. 1998). We can conclude that genes with different evolutionary origins are faced with the same evolutionary forces once they are isolated on the Y chromosome.

The acquisition of a male-specific function may be investigated by comparing Y-borne male-specific genes with their ubiquitously expressed X-borne partners. Acquisition of a male-specific function necessitates a change in the expression profile and perhaps in gene structure and binding partners. Y-borne copies show many structural changes, including internal amplification (Delbridge *et al*. 1999). Acquisition of a male-specific function by a gene on the Y has been studied by comparing the ratio of synonymous to non-synonymous nucleotide substitutions, with the tentative conclusion that...
directional selection could explain an excess of changes that alter an amino acid (Wyckoff et al. 2002).

*SRY* has also been shaped by the same evolutionary forces (reviewed by Graves 1998). This gene appears to be a truncated copy of *SOX3*, evolving in the first place by deletion of sequences outside the HMG box that binds and bends DNA. It shows a high mutation rate, typical of other genes on the Y. Differences in expression pattern, and even size and amino acid composition between human and mouse *SRY* protein, imply that in rodents this gene has undergone significant recent variation in structure and function. In one marsupial family, an intron has been created *de novo* in *SRY* (O’Neill et al. 1998).

In the long-term, only those genes that contribute to male fitness might be expected to survive on the Y. This structure explains why more than half of the genes on the human Y, and most of the genes on the mouse Y, are expressed exclusively in the testis, and presumably have roles in testis differentiation or function. Thus the ‘coherence’ of the Y (Lahn and Page 1997) has an evolutionary, not a functional, explanation.

### The use-by date of the Y chromosome

As discussed above, we have very strong evidence that genes on the Y chromosome are under constant bombardment, and are being lost at a significant rate. The human Y chromosome retains only 45 genes of an original 1438. Thus, 1393 genes have been lost from the Y over the last 300 million years at most, a rate of loss of at least 4.6 genes per million years.

At this rate, the last 45 genes will all be gone within another 10 million years or so.

This may be a conservative estimate. There is an extremely high rate of recurrent deletion of a 1.6-Mb region that contains genes required for spermatogenesis (Repping et al. 2003a; Tyler-Smith and McVean 2003), such that this mutation, although conferring infertility, is maintained as a polymorphism in the human population. From the observation that 1% of men are infertile because of a Y deletion, Sykes (2003) argued that human fertility will decay to 1% of its present level in 125,000 years. There is some evidence that as the Y chromosome is further degraded, it becomes even more unstable. Several male babies born from intracytoplasmic sperm injection (ICSJ) have more Y deletions than their sub-fertile fathers (Kent-First et al. 1996). Thus the Y chromosome could disappear much more rapidly than I predicted.

However, some genes on the Y are clearly essential for male development and function. It might be thought that genes that are essential for male reproduction cannot disappear from the Y. This is clearly not the case, for we have examples in which male-specific genes – including even *SRY* – have been lost in one mammal species or another.

For instance, *Ube1Y* is testis-specific in mice and required for spermatogenesis, but its homologue has been recently degraded and lost from the primate Y chromosome (Mitchell et al. 1998). Its function must presumably have been taken over by other genes, perhaps *UBE1X* or autosomal genes from the same ubiquitin-binding enzyme family. In the same way, there is a testis-specific Y-borne copy (*ATRX*) of the X-borne sex-reversing gene *ATRX* in marsupials, but not eutherians (Pask et al. 2000). Its function has presumably been taken over either by *ATRX* or by a related gene.

Even the sex-determining gene *Sry* has been lost from at least two rodent lineages; two species of mole voles of eastern Europe (Just et al. 1995) and the spinous country rats of Japan (Sutou et al. 2001). The mole voles, *Ellobius lutescens* and *E. tancrei*, both lack a Y chromosome and have no *Sry* gene (Just et al. 1995). It is easy to imagine that another gene could take over the control of testis determination, since there are several female-to-male sex-reversal syndromes. Thus, even genes essential for testis determination may be lost from the Y, and presumably their function would be usurped by genes elsewhere in the genome that act in the same sex-determining and spermatogenesis pathways.

### Conversion of the degenerate Y chromosome

Has the Y chromosome entered a terminal stage of degeneration and genetic impotence? The doleful prediction that the human Y will be gone in 10 million years (Graves 2002) has been vigorously opposed, and the recent news that the human Y chromosome does, after all, undergo a type of recombination (Rozen et al. 2003; Skaletsky et al. 2003) has been greeted with some relief. The human Y, it transpires, has unusual repetitive structures (palindromes) that permit genetic interaction within the Y. Perhaps gene conversion within loops formed by large palindromic sequences might compensate for the lack of recombination between different Y chromosomes (Rozen et al. 2003; Skaletsky et al. 2003). Perhaps, then, genes within palindromes can withstand the forces of degradation by making more copies of themselves, and continually correcting their sequences.

Complete sequencing of the human Y (Skaletsky et al. 2003) revealed eight palindromic regions, some very large, that read the same forwards and backwards (Fig. 2). The lengths of the arms range from 9 kb to 1450 kb and pairs of arms are separated by an unpaired spacer of 2–170 kb. Arrays of amplified functional male-specific genes are concentrated within these palindromes. These copies showed surprisingly little sequence divergence given the high rate of variability of genes on the Y, suggesting either that they amplified very recently, or that there was some kind of homogenisation mechanism. Some of the palindromes have also been shown to be present on chimpanzee, bonobo and gorilla Y chromosomes (Rozen et al. 2003), so are at least a few million years old.

Palindromes can make internal hairpin loops within a single Y chromosome, within which internal pairing and recombination could take place. Near identity of sequences...
on the two palindrome arms could be explained by a high frequency of gene conversion between homologous genes on the two arms. Gene conversion occurring between alleles on homologous chromosomes at meiosis non-reciprocally replaces one allele with the other (Weaver 1999), and would have the effect of homogenising sequences between the arms. The frequency of conversion required to offset the high mutation rate of sequences on the Y was calculated to be 600 per generation (Rozen et al. 2003). Gene conversion within the palindromes of the Y could occur at meiosis or mitosis or both. Conversion was claimed to offer the Y chromosome a way out of its unrelenting decline and stave off its inevitable disappearance (Rozen et al. 2003; Skaletsky et al. 2003).

What effect will gene conversion within palindromes have on the evolutionary forces that degrade the Y? Does the Y chromosome engage in sexual reproduction after all, with its capacity to renew and repair the genome?

Gene conversion occurring between gene copies on either arm of the palindrome would non-reciprocally replace one copy with another. If a copy on one arm is mutated, it could be replaced by an active copy. Clearly, if mutated copies of a multi-locus gene are continually converted back into active copies, the numbers of active copies will increase, and the Y will, indeed, be saved. However, gene conversion is not directional. The process is just as likely to substitute a mutated copy for an active copy than it is to resurrect inactive copies. Overall, it is hard to see how gene conversion within palindromes could increase the number of active copies of genes on the Y. In the absence of some mechanism that biases the direction of conversion, conversion would be expected to negate the cushioning effect of having large numbers of duplicates. A cluster of copies within an amplicon would be all good, or all bad. Once the cluster was, by chance, converted into a set of mutated copies, the whole cluster would cease to be functional.

In fact, the numerous inactive pseudogenes, as well as the fifteen families of transcribed but untranslateable transcripts within palindromes, suggests that there are more casualties of the process than successes. What we may be seeing, among the multi-copy testis-specific genes in palindromes, are the very few survivors of a random process that homogenises sequences among copies – in either direction.

It is therefore left to selection to sort out the good Y chromosomes from the bad – and as we have seen, drift and hitchhiking may confound the most rigorous selection. Will the occurrence of intra-Y gene conversion halt genetic drift or make hitchhiking any less likely? I see no reason why intra-Y events will affect drift or selection, other than by increasing the amount of variation for these mechanisms to work on. A Y chromosome will still be genetically isolated and act as a single supergene, being lost or retained at a roll of the genetic dice.

Thus, I would argue that gene conversion within palindromes is more like genetic masturbation than real sex. It does not offer interaction between different Y chromosomes, which is essential for the genetic health of a region of the genome.

**Will the disappearance of the Y chromosome mean the disappearance of men?**

With the inevitable loss of the human Y, will males disappear? Will humans simply become extinct, or will we adopt some form of parthenogenesis, in which female eggs develop without being fertilised by sperm? This Amazonian scenario, though much touted in the popular press, simply cannot happen in mammals.

In reality, we are locked into sexual reproduction by our system of imprinted genes – at least a hundred of which are active only if they come from the mother, or only if they come from the father. Embryos constructed from two maternal pronuclei die because they lack a developed extraembryonic region: cells with two paternal pronuclei die because embryonic development doesn’t get very far (Surani et al. 1990). Whether or not genomic imprinting evolved to prevent asexual reproduction in mammals is a moot point, but in any event, parthenogenesis is definitely not an option for humans and other mammals. Barring cloning, males are therefore absolutely required for human reproduction.

Fortunately, a male-less world is not a necessary consequence of losing the Y chromosome. For instance, the mole vole manages to have males and females without the benefit of a Y chromosome or the Sry gene (Just et al. 1995). The presence of roughly equal proportions of male and female offspring implies that these creatures have invented a new form of genetic sex determination. Somewhere in the mole vole genome, a new sex-determining gene must have emerged.

It will be important to discover the identity and location of this new sex-determining gene in the mole vole genome. Is it one of the genes that we know to be involved in the sex-determining pathway? Or is a completely different pathway? The hunt is on for the new sex-determining gene by looking for sex linkage among candidate genes (Baumstark et al. 2001). Not only is it of intrinsic interest to see how the control of sex determination can flip from one mode to another, but it might uncover a new gene in the human sex-determining pathway, and one that may be involved in human sex-reversal syndromes.

It is not at all hard to accept that a new gene might take over mammal sex determination, because we know of several XY female and XX male syndromes in humans in which a mutant gene has short-circuited the normal testis-determining pathway. For example, haplo-insufficiency for SOX9 or DMR1, deletion of ATRX and duplication of DAX1 prevent testis determination in XY patients. Duplication of SOX9 produces testis development in XX male patients (Huang et al. 1999) and the oddsex line of XX male mice has an alteration...
Will gene conversion save the Y chromosome?

Reproduction, Fertility and Development

There may be several different potential genetic solutions to the problem of Y instability and the loss of SRY. It is interesting to speculate on how different sex-determination mechanisms in different populations might interact. There are likely to be intersexes or infertility among hybrids of these two species, which may be the preconditions for establishment of a species barrier. Maybe this is what happened to differentiate the two species of Y-less mole voles that differ in having either two X chromosomes or a single X chromosome (Just et al. 1995). Was the evolution of alternative sex-determining genes a speciating event?

What if different sex-determining genes take over from SRY in different human populations? What happens if wood lemming woman meets mole vole man (D. Fox, personal communication)? Or XX Sox9 duplication man meets XY Dax1 duplication woman? Will a testis-suppressor gene on a neo-X over-ride a testis-determining neo-Y? Or vice versa? Hybrid intersexes or infertility in different human populations could conceivably provide the preconditions for the creation of new species of hominids.

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