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# Is the Y chromosome disappearing?—Both sides of the argument

Darren K. Griffin

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**Abstract** On August 31, 2011 at the 18th International Chromosome Conference in Manchester, Jenny Graves took on Jenn Hughes to debate the demise (or otherwise) of the mammalian Y chromosome. Sex chromosome evolution is an example of convergence; there are numerous examples of XY and ZW systems with varying degrees of differentiation and isolated examples of the Y disappearing in some lineages. It is agreed that the Y was once genetically identical to its partner and that the present-day human sex chromosomes retain only traces of their shared ancestry. The euchromatic portion of the male-specific region of the Y is  $\sim 1/6$  of the size of the X and has only  $\sim 1/12$  the number of genes. The big question however is whether this degradation will continue or whether it has reached a point of equilibrium. Jenny Graves argued that the Y chromosome is subject to higher rates of variation and inefficient selection and that Ys (and Ws) degrade inexorably. She argued that there is evidence that the Y in other mammals has undergone

lineage-specific degradation and already disappeared in some rodent lineages. She also pointed out that there is practically nothing left of the original human Y and the added part of the human Y is degrading rapidly. Jenn Hughes on the other hand argued that the Y has not disappeared yet and it has been around for hundreds of millions of years. She stated that it has shown that it can outsmart genetic decay in the absence of “normal” recombination and that most of its genes on the human Y exhibit signs of purifying selection. She noted that it has added at least eight different genes, many of which have subsequently expanded in copy number, and that it has not lost any genes since the human and chimpanzee diverged  $\sim 6$  million years ago. The issue was put to the vote with an exact 50/50 split among the opinion of the audience; an interesting (though perhaps not entirely unexpected) skew however was noted in the sex ratio of those for and against the notion.

**Keywords** Y chromosome · evolution · sex determination · dosage compensation · palindromes

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Responsible Editor: Tariq Ezaz and Jenny Graves.

Comment on a debate between Jennifer Marshall Graves and Jennifer Hughes at the 18th International Chromosome Conference Manchester, August 31, 2011.

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## Abbreviations

BAC	Bacterial artificial chromosome
Mb	Megabase pairs
MSY	Male-specific region of the Y chromosome
<i>RBMY</i>	RNA-binding motif gene on Y chromosome
<i>SRY</i> or <i>sry</i>	Sex-determining region on the Y (upper case human lower case rodent)

## Foreword

On May 24, 2008 Manchester played host to the largest post war crowd for a boxing match in the UK (55,000). Local boy Ricky “the Hitman” Hatton defeated Mexico’s Juan Lazcano by a unanimous decision in a hard fought contest that went the distance. On August 31, 2011 Manchester again was the venue of a monumental battle that also went the distance. The gloves were off but the sparring more genteel as Jenny Graves took on Jenn Hughes in front of 300 delegates at the 18th International Chromosome Conference. Up for debate was the issue of whether the mammalian Y chromosome a symbol of masculinity in both the scientific and popular press, is doomed in evolutionary terms. Given that 50% of the audience possessed one (per cell) of these fundamentally important, but nonetheless (for the most part) genetically inert, lengths of chromatin, there was more than a passing interest from all concerned. Readers of Chromosome Research will not need to guess on which side of the argument each of the Jennifers expressed their opinions but, to the best of my knowledge, this is the first time that two of the leading protagonists have squared up in person in front of an audience of chromosome researchers. What follows is a personal exposition of a session that I was delighted to chair as it had all the elements of what makes science so fascinating: The highest quality research, healthy debate, informed opinion, controversy and public interest.

## Background

Sex chromosome differentiation is clear example of homoplasmy (convergence). It has occurred several times independently during evolution and does not necessarily appear to favour the chromosome carrying a male-determining locus as the one that will ultimately degrade; in mammals however, the *SRY*-bearing chromosome is the one that underwent degradation. Several species have only slightly differentiated sex chromosomes—the originals are pythons, among “Ohno’s snakes” (Ohno 1969), but many more have been described including ratite birds (Takagi and Sasaki 1974; Nishida-Umehara et al. 2007), tilapia (Campos-Ramos et al. 2001; Harvey et al. 2002), and European tree frogs (Stöck et al. 2011). Either sex can

be the heterogametic one, and ZW systems (where the female has unlike sex chromosomes) are commonplace. Birds are probably the best-cited example, but Lepidoptera (butterflies and moths), snakes, and some fish and reptiles also have ZW systems. In some groups of animals, both ZW and XY systems are reported in the same groups (Organ and Janes 2008; Ross et al. 2009) even at the level of the same genera (Campos-Ramos et al. 2001; Griffin et al. 2000; Harvey et al. 2002; Takehana et al. 2007) or species (Ogata et al. 2007). While there are a number of examples of fish (Kondo et al. 2004; Peichel et al. 2004), insects (Bachtrog and Charlesworth 2002; Benatti et al. 2010), and plants (Liu et al. 2004; Filatov 2005) with novel sex chromosome systems close to the beginning of the degenerative process, neo-sex chromosomes have been identified in very few mammalian, avian or insect species (Zhou et al. 2008; Pala et al. 2011; Carvalho and Clark 2005).

It is generally agreed by all parties therefore that the Y chromosome was once genetically identical to its partner and a homologue in every sense. The present-day human X and Y chromosomes retain only traces of their shared ancestry as identical autosomes. The euchromatic portion of the male-specific region of the Y chromosome (MSY) is roughly 1/6th the size of the X chromosome and has only ~1/12th of the number of genes (Skaletsky et al. 2003; Ross et al. 2005). In other words, there is little doubt that, in essence, the Y chromosome is a degraded X (Ohno’s hypothesis). Sex chromosome evolution (at least for the XY mammalian system) is a common, if not inevitable, consequence of the evolution of genetically determined sex. While genetic sex determination is by no means the only way of promoting dioecy (phenotypically distinct males and females) it is an effective one, and sex chromosome differentiation often follows the evolution of a sex-determining locus such as *SRY*. A cycle of events that near-obliterates the Y chromosome ensues; this includes reduction in recombination around the sex-determining region that could have initially been a consequence of a de novo stochastic expansion of heterochromatin (Griffin et al. 2000). In any event, the presence of a sex-determining locus drives a series of events—recombination reduction—loss of euchromatin—expansion of heterochromatin—loss of recombination and so on; events that are bad news for the Y (Graves 1995).

The big question however is whether this degradation will continue or whether it has reached a point of equilibrium where it can go no further. Such was the nature of this debate and clear and concise arguments were presented both for and against.

The case for

Jenny Graves opened the proceedings with her argument of why the Y was headed for oblivion. Jenny assured us that she was no “male basher” and that she had no ulterior motives in taking her stance, pointing out that neither of the protagonists possessed a Y chromosome in any of their cells. Rather, the argument was based on many years of research into the evolution of chromosomes (including the sex chromosomes) in a number of species. The venerable theory that sex chromosomes evolved from an ordinary autosomal pair as the Y (or W) degrades progressively (Muller 1914) is confirmed by observations in vertebrates, invertebrates and even plants. Fundamentally, the argument is that the Y chromosome has been degenerating for millions of years and it is only a matter of time before it disappears completely. Jenny explained that the human X is a decent-sized chromosome bearing ~1,000 protein-coding genes (Ross et al. 2005), over-endowed in “brains-and-balls” genes involved in reproduction and intelligence (often both). The tiny Y is a genetic wasteland, full of “junk” and bearing only 45 genes that code for different proteins, most of which are active only in the testis.

There is overwhelming evidence of considerable homology between the mammalian X and Y chromosomes. Most of genes on the Y chromosome have orthologues on the X; however, the gene content of the Y differs somewhat between mammals. That is, some genes have “dropped out” in certain lineages whereas other genes have disappeared in other phylogenetic groups (Graves 2006). It is clear that even genes with an important function can drop out and be replaced, however if all disappear, the Y chromosome is free to be lost. In terms of the fate of genes on the Y chromosome, there are a number of possibilities (Graves 1995):

- Some remain intact and functional (mostly on the pseudoautosomal region)
- Some acquire mutations that make them less active

- Some are inactivated completely and become pseudogenes
- Some “get desperate” and make more copies to compensate for mutations
- Most completely disappear
- A small number are introduced to the Y chromosome from other autosomes

Of those that remain, nearly all have a function in male fertility or sex determination. Their X-borne partners, from which they evolved, have been described as “brains and balls genes” as they are predominantly expressed in brain and testis (Graves 2001).

Jenny proposed three models that describe the Y chromosome (Graves 2000)—the “dominant Y” exerting a massive influence over the phenotype despite its small size, the “selfish Y” grabbing genes from other autosomes, and the “wimpy Y,” a shadow of its former self. We know the dominant Y model describes only the influence on male phenotype of a single gene *SRY*, which alone can induce testis differentiation and switch on hormones that masculinize the embryo. The “selfish” model well describes the *Drosophila* Y chromosome, which originated as a heterochromatic element and imported copies of many fertility genes (Carvalho and Clark 2005); however, this describes only a handful of genes on the mammalian Y, as most of its genes have a homologue on the X chromosome. Clearly, the model that best fits is therefore the “wimpy Y”.

The key to understanding why the “wimpy Y” will eventually disappear lies in the consideration of why it degrades at all. Books have been written on this topic but the basic premise is that high variation on Y chromosome leads to many mutations, deletions and insertions. Jenny pointed out that the Y chromosome is forever passed between generations in a testis and never in an ovary; the testis is dangerous place to be as there are many mitoses and opportunities for DNA damage, also repair is lacking (Aitken and Graves 2002; Shimmin et al. 1993). There is no opportunity for salvation because selection does not work very well due to the absence of genetic recombination (Charlesworth and Charlesworth 2000). Robbed of the ability to select on single loci, nature must select for or against the whole chromosome. Thus a good variant on a bad

Y chromosome does not have much chance of survival and a bad variant can often be carried along for the ride (Rice 1987a).

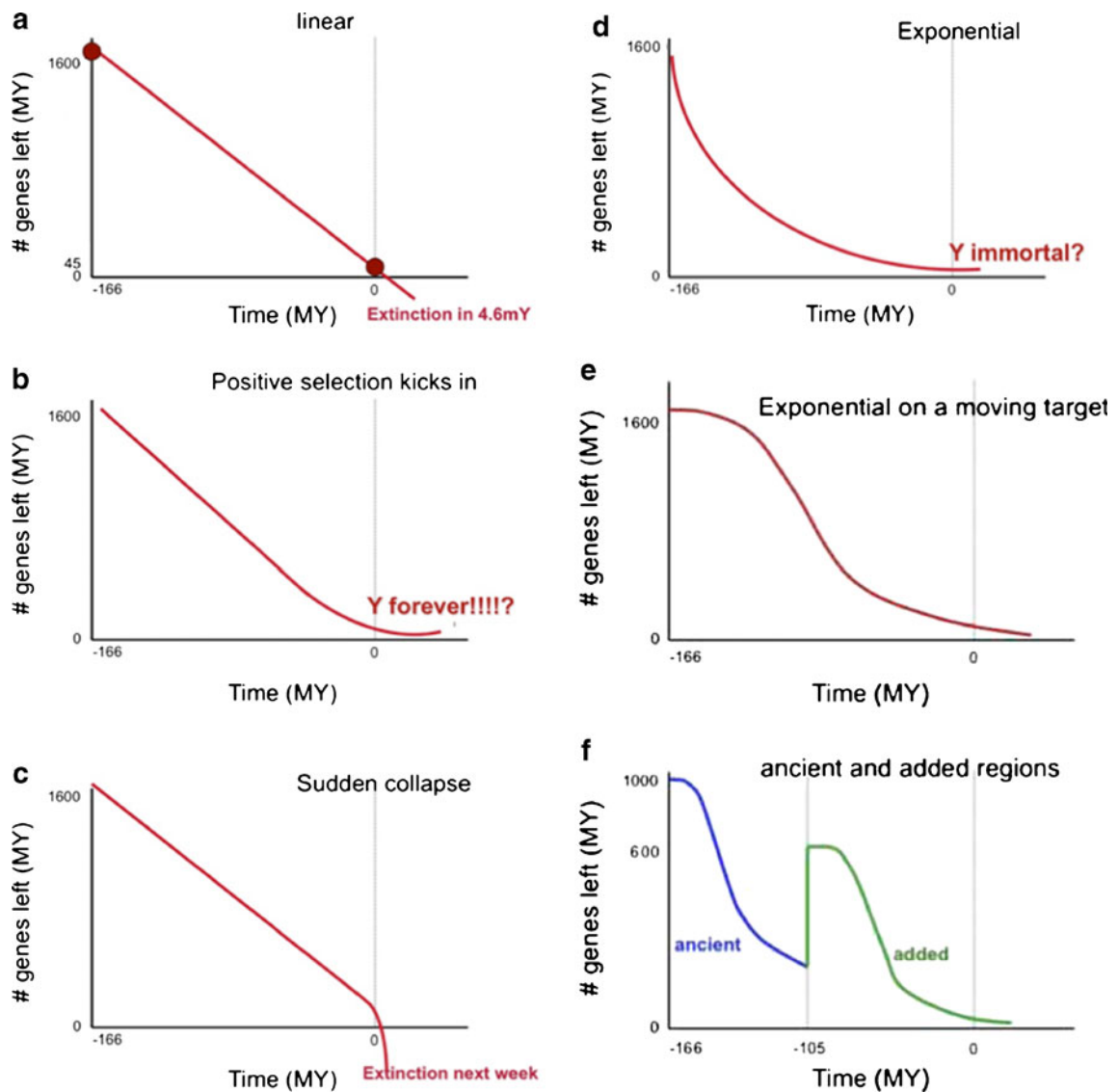
The Graves lab has studied many species including humans, elephants, marsupials, monotremes, reptiles, and even frogs. Humans and elephants share a common ancestor that lived 105 million years ago; however, the X chromosome remains largely conserved between the two in gene order as well as gene content. Comparative mapping of human X genes in marsupials identified an X-conserved region (mostly comprising the q arm) and an X-added region (the most part of the p arm), which is autosomal in marsupials. Not counting the pseudoautosomal regions, the human Y contains some genes (7) deriving from the X-conserved region but most (12) from the X-added region. The kangaroo Y on the other hand contains around 12 genes all with “brains and balls” X homologues on the ancient conserved X. Looking further into the evolutionary past, it is clear that the mammalian XY system is relatively young in that birds and reptiles have a variety of other systems, one of which is shared among distantly related species, so may be ancestral. The observation that some distantly related reptiles (a gekko and a turtle) have a bird-like ZW suggests this was ancestral to reptiles. Even in monotremes, the complex sex chromosome system is orthologous to the ancestral ZW chromosomes, not the XY seen in marsupials and eutherian mammals, suggesting that this ZW system was ancestral to all amniotes (Graves 2006, 2008). This dates the evolution of the mammalian XY system relatively precisely to 160 million years ago, the time at which therian mammals diverged from monotremes. Thus the human XY and *SRY* are very young in evolutionary terms.

The question therefore arises of how long the Y chromosome will last given its current rate of decay. Jenny used the most recent estimates of the numbers of genes on the human X to deduce that the ancestral Y once had about 1,700 genes on it. It now has only 45. If we assume a linear rate of loss (given that we only have two points of reference) it is predicted that the Y chromosome will disappear in 4.6 million years (Fig. 1a). There are of course possibilities other than a linear degradation (Graves 2006). The first assumes an initial linear loss but with the graph “levelling out” as some

Y chromosome genes are retained because they are in some way “useful” (Fig. 1b). This is unlikely to provide a complete protection against loss because there are genes that are on the human Y that are present in some mammalian lineages but not others. A second model (Sykes 2004) is that a complete collapse is imminent (Fig. 1c). Indeed this has already happened in that two lineages of rodents have already survived the complete loss of the Y chromosome. One of these is the Japanese spiny rat (genus *Tokudaia*) (Kuroiwa et al. 2010). Of the three species that inhabit a group of islands off the coast of Japan, one has retained the Y chromosome (the Okinawa spiny rat *Tokudaia muenninki*), whereas the other two (the Amami spiny rat *Tokudaia osimensis* and the Tokunoshima spiny rat *Tokudaia tokunoshimensis*) have lost their Y chromosomes completely and do not appear to have *sry*. Exponential models (e.g., Fig. 1d and e) based on a reduction of target size are flawed because the target starts off being very tiny (one gene); a sinusoidal curve was proposed that can predict both the loss and persistence of the Y chromosome. These forces, and the factors that affect them, are explored in depth by more formal modeling (Bachtrog 2008). A two-stage sinusoidal degradation of first the X-conserved, and then the X-added regions has been proposed as the most realistic model (Graves 2006; Fig. 1f).

The “Graves prediction” that the Y will be lost in around 4.6 million years of course raises the question of whether the demise of the Y chromosome will mean the loss of males as well. An all-female race reproducing parthenogenetically (as do some lizards) is unlikely because of genomic imprinting and, in all likelihood, new sex determining genes will evolve and sex chromosome differentiation will start again, as it has evidently done in spiny rats and mole voles. Could this happen in humans? Perhaps it already has in some populations, Jenny laughed; if so, mating between a “spiny rat” male and an XX female might present a war of the sex determining systems that results in infertile offspring. This could pose a reproductive barrier that leads to the divergence of a new hominid species, as has happened in the spiny rat and the mole vole. If humans do not become extinct, new sex determining genes and chromosomes could evolve, maybe leading to the evolution of new hominid species.

Looking at the big picture then, Jenny asserted that whatever trajectory we choose, the Y will inevitably



**Fig. 1** Various models predicting the demise of the Y chromosome. **a** The linear model predicting loss in 4.6 million years, **b** the “Y forever model” proposed by Jennifer Hughes, **c** the “sudden collapse” model, **d** an exponential model

predicting a slower decay of the Y chromosomes, **e** model of the degradation of the ancient and added regions of the Y similar to Bachtrog (2008)

disappear (somewhere between three weeks and infinity) for the following reasons.

1. The Y chromosome is subject to higher rates of variation and inefficient selection.
2. There is evidence from across the animal kingdom (not only in mammals), and even in plants, that Ys (and Ws) degrade inexorably.
3. There is evidence that Y in other mammals has undergone lineage-specific degradation.

4. There is evidence that the Y has already “gone nuts” or completely disappeared in some rodent lineages.
5. There is evidence that there is practically nothing left of the original human Y and the added part of the human Y is degrading rapidly.

The case against

Jenn Hughes thanked and praised her rival for an excellent talk but sought to expand on reasons why

she was wrong. Her assertions are based on the study of the Y chromosome sequences of three primates (human, chimpanzee, and rhesus macaque) covering 25 million years of evolution (Skaletsky et al. 2003; Hughes et al. 2010; Hughes, personal communication). In the described research, the primate Ys were purposely sequenced by the traditional “BAC-by-BAC” approach, partly because, in many species, a female was chosen as the reference individual and partly because shotgun sequencing gives an inadequate assembly of the Y chromosome.

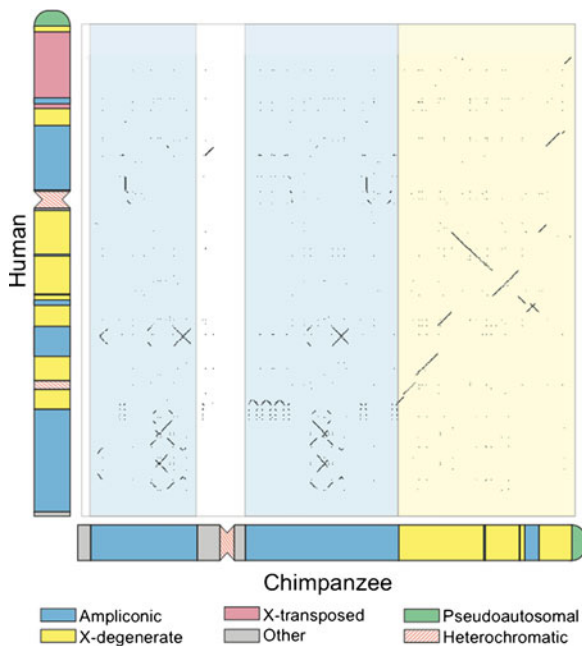
Jenn argued that there can be no doubt that the mammalian (including the human) Y chromosome can be thought of, at least in part, as a “rotting X.” There are ~1,000 genes on the 180-Mb X chromosome (Ross et al. 2005), but only 78 genes on the 23 Mb Y (Skaletsky et al. 2003). The degeneration on the Y is a consequence of its lack of a meiotic recombination partner over most of its length. The suppression of recombination between the X and Y was selectively advantageous at first, as the proto-Y chromosome became a good place for male-benefit genes to land, and subsequent suppression of recombination kept these genes linked to the male-determining *SRY* locus (Rice 1987b).

The human Y chromosome was the first Y chromosome from any species to be fully sequenced (Skaletsky et al. 2003). It is dominated by a large heterochromatic region, but Jenn and the laboratory of David Page focus on the euchromatic remainder of the “male-specific Y” (MSY; excludes the small pseudoautosomal regions that still recombine with the X) that is of most interest to evolutionary studies. The euchromatic portion of the human MSY is comprised of three discrete sequence classes. The “X-transposed” region is a ~3-Mb block of gene-poor sequence that was transferred from the X to the Y about 3–4 million years ago (Page et al. 1984). The “X-degenerate” regions can be thought of as the rotting-X component of the MSY and account for less than half of its total euchromatic content. The X-degenerate regions contain 16 intact single-copy genes, most of which have ubiquitous expression patterns. Finally, the “ampliconic” or repeat-rich regions that make up the largest fraction of the MSY euchromatic sequence are densely populated with multicopy genes that are expressed exclusively in the testis, implying a role for these genes in spermatogenesis. All of the X-degenerate genes and

some of the ampliconic genes derive from shared X–Y ancestry. A number of the ampliconic genes have been transposed from autosomes (Saxena et al. 1996; Lahn and Page 1999) or have other origins.

Jenn then addressed the question of what is the fate of the genes on the Y that, in the absence of normal meiotic recombination, are at risk of becoming obliterated by mutation and drift? Insights from a detailed analysis of the structure of the human Y sequence imply that the Y has some tricks up its sleeve to counteract the decay process. Much of the ampliconic sequence is made up of palindrome structures that are closely spaced inverted repeats sharing >99.9% identity (Skaletsky et al. 2003). The process of gene conversion, or non-reciprocal recombination, maintains this high level of identity within the repeat units and may serve to protect the integrity of the critical spermatogenesis genes that reside within these repeats, even in the absence of “normal” meiotic recombination with a homologue (Rozen et al. 2003). In other words, the ampliconic genes persist by recombining with themselves however, the fate of the single-copy genes on the Y chromosome, which are not protected by gene conversion, is still in question.

Jenn then turned to the chimpanzee Y sequence as it gives insight into the recent evolutionary history of the primate Y chromosome and its genes. Overall, the Y chromosomes of human and chimpanzee, whose lineages separated 6 million years ago, are strikingly divergent. While human chromosome 21 and its chimpanzee counterpart have remained largely unaltered structurally (i.e., the chromosomes are colinear) during the same time period (Watanabe et al. 2004), the respective Y chromosomes have undergone multiple rearrangements (Fig. 2; Hughes et al. 2010). There are multiple large-scale inversions, duplications, insertions, and deletions evident in the Y-chromosome comparison. To consider each euchromatic sequence class separately, the level of rearrangement is notably higher in the ampliconic regions compared to the X-degenerate regions (Fig. 2). In addition, the amount of species-specific sequence, or sequence present in one species but not the other, is dramatically higher in ampliconic vs. X-degenerate sequences (~50% vs. ~9%). Although the total size of the chimpanzee Y is much smaller because it is lacking the large heterochromatic region found in human, the ampliconic sequence is considerably



**Fig. 2** Dot plot analysis of human and chimpanzee MSYs. Plot is generated by comparing human (represented on *Y*-axis) and chimpanzee (represented on *X*-axis) MSY sequences and a dot is plotted for every 100-bp window corresponding to 100% identity between sequences at corresponding positions. Schematic diagrams of human and chimpanzee Y chromosomes are shown with color coding to indicate sequence classes, as indicated. Color shading within plot corresponds to sequence classes in chimpanzee sequence to contrast degree of rearrangement/sequence conservation within predominantly ampliconic (*at left*) and X-degenerate (*at right*) regions

larger and more complex in chimpanzee. The proportion of the MSY sequence that is ampliconic is 57% in chimpanzee, compared to only 45% in human, and the chimpanzee MSY has more than twice the number of palindromes found in human.

Jenn then returned to the question of gene loss. A comprehensive comparison of the gene contents of the human and chimpanzee MSYs reveals that there has been no gene loss from the human lineage over the past 6 million years or since the time of divergence of the human and chimpanzee lineages (Hughes et al. 2005, 2010). This conclusion can only be reached because two complete MSY sequences were compared and the chimpanzee assembly and annotation were not dependent on knowledge of the human MSY sequence, nor gene content. Therefore it is evident, she argued, that the chimpanzee MSY contains no genes that are missing in the human sequence. Rather than losing genes at a constant rate

(or 10 genes per million years as predicted by the linear decay model), the human MSY has held steady for 6 million years (Fig. 3). The chimpanzee MSY, on the other hand, has suffered considerable gene loss in the same time frame (Hughes et al. 2005, 2010). A total of six genes have been lost in the chimpanzee lineage (Fig. 3). What can account for this acceleration in decay? Perhaps the process of genetic hitchhiking, where a deleterious mutation gets dragged along to fixation in a population if it is linked to a beneficial mutation, has come into play in chimpanzee. The chimpanzee has a multimale–multifemale mating system (Dixson 1998), so sperm competition is intense. Therefore, in chimpanzee, positive selection on a mutation in one gene that greatly increases spermatogenesis output might be so strong that it overshadows the relatively weaker purifying selection acting on another MSY gene that has a more subtle phenotypic effect (Hughes et al. 2005, 2010).

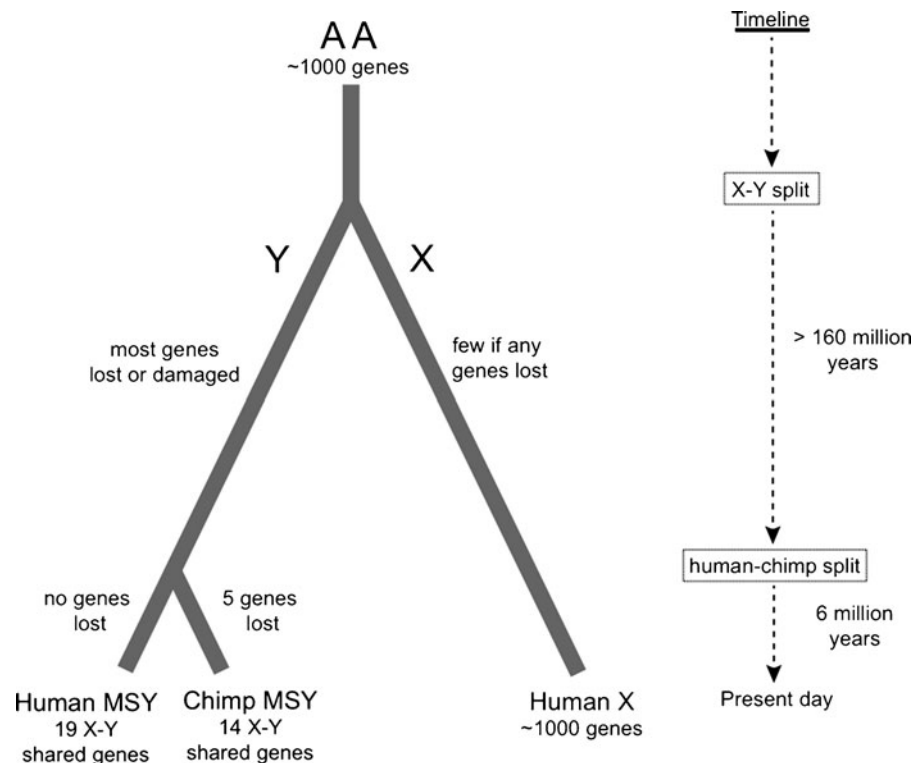
Jenn then described some recent work on completion of the MSY sequence of the rhesus macaque (Hughes personal communication), an Old World monkey whose lineage separated from that of human ~25 million years ago. This, she pointed out, gives an even deeper glance back in evolutionary time. Surprisingly, the human Y has held up incredibly well over this expanded time frame. High-quality sequences of a number of MSYs from even more distant mammals, including marmoset, mouse, rat, bull, and opossum are in process, promising to illuminate the history of gene loss and gain on the MSY over close to its entire history, which should allow us to make even more reliable predictions about the fate of the human Y.

In summary therefore, Jennifer Hughes assert that the Y chromosome is not disappearing because:

1. It has not disappeared yet and it has been around for hundreds of millions of years.
2. The Y chromosome has shown it has ways to outsmart genetic decay in the absence of “normal” recombination.
3. Most of the genes on the human Y exhibit signs of purifying selection over millions of years primate evolution and within the past 100,000 years of human evolution.
4. The human Y has added at least eight different genes, many of which have subsequently expanded in copy number, over the course of its history.



**Fig. 3** MSY gene loss in the human and chimpanzee lineages over the course of sex chromosome evolution. Tree represents evolutionary relationships between autosomal progenitors of mammalian sex chromosomes (AA) and present-day human X and human and chimpanzee Y chromosomes. Gene contents for each chromosome are indicated. Timeline of major events is shown at right (not drawn to scale)



5. The human Y has not lost any genes since the human and chimpanzee lineages diverged ~6 million years ago.

#### The rebuttals

Each candidate was given 5 min to rebut the other's argument. Jenny Graves argued that, in analyzing the relationship between primates, we are looking at a very tiny evolutionary interval and that we need to consider the issue in a broader evolutionary context. Harbingers of our future are two rodent lineages that have already lost both the Y and *sry* (the aforementioned spiny rat and the mole vole). Moreover, they provide good examples of the Y chromosome "clinging on to life." One spiny rat species *T. muenninki*, retains a Y containing *sry* but this does not bind DNA very well so, to compensate, has made 40–50 copies of itself in a "last gasp" (Murata et al. 2010). An even more extreme view of our future is provided by some *Drosophila* species that are on their third Y chromosome. *Drosophila melanogaster* has already completely lost its Y chromosome, which was substituted by a selfish blob of heterochromatin; in other species

this blob has been translocated to an autosome, which, in turn is being rapidly degraded (Carvalho and Clark 2005; Graves 2005). This complete loss and substitution seems to be the endpoint common to all animals—vertebrates and invertebrates—with differentiated sex chromosomes—why would the human Y be any different? Gene conversion is not directional, so can result in conversion of a mutant to an undamaged copy, but equally can result in conversion from a good copy to a mutant copy and, once it's gone, it's gone, the process is irreversible—what Jenny calls "doubles or quits" kinetics that results in a jerkier degradation, but degradation nonetheless. The results of this process can be seen in the detritus on palindrome arms; for instance, the human Y has 28 copies of the *RBMY* gene but only two of these are active. Palindromes and gene duplication by themselves will not save the Y without selection kicking in and we have already seen that selection does not work very well. It may be easier to recruit another gene copy on an autosome; for instance, *RBMY* and its X homologue have spawned several autosomal copies, one of which is active in testis (Lingenfelter et al. 2001) just standing by in case the spermatogenesis factor *RBMY* is eliminated.

Jenn Hughes however argued that gene conversion can preserve Y genes. Natural selection will swiftly remove Ys that contain mutated copies of genes that play important roles in male fertility. There is clear evidence from the comparison of orthologous palindrome sequences in chimpanzee and human that palindromes are indeed evolving significantly slower than adjacent sequences (Rozen et al. 2003), implying the existence of biased gene conversion (or the tendency to maintain the status quo). In addition, recent studies that utilize population genetics and simulation-based models indicate that even low levels of gene conversion are sufficient to maintain the integrity of Y-linked genes (Connallon and Clark 2010; Marais et al. 2010). Furthermore, even genes that do not experience gene conversion—the single-copy, X-degenerate genes—are evidently under strong purifying selection in the human lineage. From the human–chimpanzee comparison, it is clear that there has not been any decay among these genes in at least 6 million years. The steady state in human has been largely maintained for at least 25 million years, as evidenced by the comparison to rhesus. Even if the age of the mammalian MSY is ~160 million years old, then the 25 million year time frame covered by this three-way comparison equates to roughly one sixth of the entire history of the MSY, which is not necessarily a “tiny” fraction. Further evidence for the ongoing operation of purifying selection on MSY genes comes from a recent study that resequenced ~100 men from a range of different ethnic backgrounds revealing remarkable coding sequence conservation within the X-degenerate genes (Rozen et al. 2009). Taken together, it is clear that most of the genes that remain on the human MSY are probably indispensable, not just for determining maleness, but for spermatogenesis and other basic biological functions, and are therefore here to stay.

### The vote

Following questions and comments from the floor, in the final *denouement* I took the opportunity to take a vote on whether delegates agreed that the Y chromosome was disappearing or not. The esteemed scientific community present was split precisely and evenly, and the contest declared an honourable draw. Interestingly however, in an audience comprising a 50:50 sex ratio, two further votes were taken. The

same question, but first for males only, then second for females only. A 2:1 ratio rejecting the notion the Y is disappearing in the first vote and a 2:1 ratio accepting the hypothesis in the second, is perhaps a reminder of the need for objectivity when making our scientific evaluations.

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