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Sex and the Single Gene: Becoming a Man is not as Easy as X+Y

By Dr. Howard Glicksman

Most of us learned in biology class that each human cell contains twenty-three pairs of chromosomes, of which there exists one pair that determines the sex of the person.

The mother's egg always provides an X chromosome and the father's sperm supplies either an X or a Y chromosome to the zygote. A person is considered, chromosomally, a female if they have an XX pattern and a male if they have an XY combination.

So far so good. But why would I qualify the statement above by saying that a person is only "chromosomally" male or female by being XY or XX respectively? Aren't they really male or female when they are XY or XX? Well…… not exactly.

It turns out that human sexual determination and development is just a little more complicated than simply observing a person's chromosomes. It is distinctly possible, due to a translocation of genetic material, to have an XX male, i.e. someone who has two X chromosomes, but who for all intents and purposes is a male. But not to be outdone, it is also possible, due to a single genetic defect, to have an XY female who has testes and no uterus, but who thinks of "herself" and is living among us as a female.

Now just when we thought we really understood human reproductive biology we're faced with this conundrum which touches on the very basics of our knowledge of life. For in addition to this, there exists other single gene defects in XY people that can result in them having ambiguous genitalia, making them impotent, and/or defects in male development resulting in sterility. Either way, having an XX or XY chromosomal pattern does not automatically guarantee a person the ability to reproduce and therefore the complexity that is inherent in this development must be addressed by Darwinists. For without this complex function of human existence, genetic variation would not have been transmitted down the line and natural selection would have been a moot point in the evolution of life.

In the Beginning

Human embryo sexual differentiation involves the development of three different tissues, all of which, on effective triggering, will ultimately result in a normally functioning male or female, who is capable of sexual intercourse and propagation of the species. These initial primordial tissues consist of:

1. The undifferentiated **gonads;** which develop into either **testes** or **ovaries**
2. The **genital duct systems**; the **Mullerian ducts** (female)-which form the fallopian tubes, the uterus and the upper vagina; or the **Wolffian ducts** (male)-which form the epididymis, vas deferens, and seminal vesicles
3. The **(uro)genital sinus, swellings, folds and tubercle;** which form either a female lower vagina, labia, and clitoris, or a male prostate, scrotum. and penis.

Here are links to the male and female reproductive systems with interactive information

- http://kidshealth.org/parent/medical/body_basics/male_reproductive.html
- http://www.kidshealth.org/parent/general/body_basics/female_reproductive_system.html

The Fork in the Road

Except for the potential contained within the genetic content of its chromosomes and the subsequent formation of primordial tissue, the human embryo is essentially asexual for the first weeks of its life. It has been shown that the undifferentiated

gonads are destined to become **ovaries** unless acted upon by **TDF** (testis determining factor), which is genetically encoded on the Y chromosome. Therefore the default sex of the human embryo is female. The information for TDF is contained in the **SRY** (sex determining region of the Y chromosome). It is the translocation of the genes encoding for the TDF to the X chromosome that can result in the abovementioned **XX male,** who ultimately will be infertile.

This TDF turns out to be the master switch for turning on the biochemical machinery that results in the formation of the **testes**. However it has been shown that there are many other genes, contained on other chromosomes, present in both human males and females, that are needed for male determination. One such gene, found in other lower organisms such as alligators and chickens, is **DMRT-1** which is located on chromosome #9. It seems to play a starring role once the master switch from the Y chromosome has been turned on. It has been shown that even if TDF is functioning, but DMRT-1 is defective or absent, the primordial gonadal tissue will form into *ovaries* and not *testes*. So having a normal appearing Y chromosome, but being absent or having a deficient DMRT-1, would be one example of how one could be an **XY female**.

So in effect, it would seem that every human embryo has the underlying biochemical machinery to have either male or female gonads and becoming male all depends on whether they have a properly functioning TDF master switch on the Y chromosome and DMRT-1 on the 9^{th}. But as we will soon see, becoming a man requires much more .

Testosterone spells M-A-L-E ?

Once the primordial gonads differentiate into testes they begin to produce and secrete two important hormones, one of which is testosterone. Testosterone is a very complex biomolecule that is derived from cholesterol. Cholesterol is ubiquitous in mammals and requires numerous specific chemical reactions to come into existence. From this point several important enzymatic reactions are needed to convert cholesterol into testosterone. The enzymes that are necessary for these specific reactions are located on several different chromosomes. A defect resulting in dysfunction of any one of these specific enzymes has been shown to result in an XY male either having ambiguous genitalia or being frankly female. Either way, each of the many enzymes necessary for adequate testosterone formation must be fully functional or else the male of the species will not be functionally able to reproduce.

All Dressed Up With No Place to Go

Just because the testes are now producing and secreting testosterone does not automatically mean that a man will now be able to reproduce. When the male of the species matures and is able to produce sperm there has to be a passageway to allow the sperm to exit the testes and be deposited in the female. Notwithstanding the male external genitalia (penis and scrotum), which will be dealt with later, the sperm first will need the male internal duct system (epididymis, vas deferens, seminal vesicles) which is derived from the Wolffian ducts, to ultimately be able to accomplish this task. The Wolffian ducts are totally dependent on testosterone for allowing them to continue to survive and develop into this male genital duct system. In fact, without testosterone, the Wolffian ducts will degenerate, usually leaving only the Mullerian ducts to develop into the female internal duct system.

As mentioned above, the default sex of the human embryo is female unless it is acted upon by certain trigger biomolecules. So far we've encountered the TDF which is located on the SRY that results in the primordial undifferentiated gonads becoming testes. And now we've just learned that unless the Wolffian ducts are stimulated by testosterone, produced by the testes, they are destined to shrivel up and die. But the testes and its production of testosterone is not wholly sufficient for producing a male who is capable of reproduction. As we will soon see, it takes more than just having testosterone to be a completely functioning male of the human species.

It Takes Two to Tango

Testosterone is indeed very important for the Wolffian ducts to develop into the male genital duct system which will ultimately facilitate the passage of sperm from the testes to the exterior of the body. But testosterone is not capable of accomplishing this feat on its own. It requires that the Wolffian duct cells contain an **androgen receptor** within the cytoplasm. A receptor that is encoded on the **X chromosome** that allows the Wolffian duct cells to identify testosterone as the trigger for further development. Without a properly functioning androgen receptor, it doesn't matter how much testosterone one has floating around in one's bloodstream, it will be biologically useless and the Wolffian ducts will in fact degenerate and not develop into the male genital duct system.

So what happens if an XY person has what is known as **Complete Androgen Insensitivity Syndrome (CAIS)**, a condition involving a deficiency of the androgen receptor, something that occurs in about 1 in 20,000 "male" births? These people become what is known as **XY females**. That's right. They will contain within themselves testes that may migrate into the groin and labia, where if found and removed, will prove their true original nature. But they will often go undetected,

appearing as totally normal females until they fail to menstruate as many of the other signs of puberty take hold. It is at this time that they will be discovered to be absent internal female organs with a vagina that leads to nowhere.

The Pause that Refreshes

Now you should be asking yourself; "What happened to the female internal organs that should have developed from the Mullerian (female) ducts if the Wolffian ducts ended up degenerating because of the lack of androgen sensitivity?" "Shouldn't they still be present since the XY female's body cannot respond to testosterone?" Actually if you think about what I have told you so far, you may be able to, in principle, figure out the answer to this question. Here are the three clues to consider from what you've just learned:

1. Degeneration of the Wolffian ducts does not automatically mean that the Mullerian ducts will develop into the female internal organs
2. The Wolffian ducts are dependent on testosterone for continued survival and development, but the default sex of the human embryo is female, which means that if left alone, the Mullerian ducts will develop into the female internal organs
3. The TDF induces the primordial undifferentiated gonads to become testes that produce and secrete two hormones, one of which is testosterone

Before moving on, take some time to think about this for a while, especially if you are a devout Darwinist. See if you can come up with the answer yourself. It may help you to better understand the complexity of what is truly involved in the development of a human male that is capable of reproduction.

"What am I, Chopped Liver?"

I hope that most of you noticed that we haven't taken into account the **other hormone** that the testes produce and secrete. Remember that the TDF from the SRY turns on among others, the DMRT-1 gene located on the 9^{th} chromosome, which results in the conversion of the undifferentiated primordial gonads into testes. The testes use cholesterol as a substrate and numerous specific enzymes located on several different chromosomes to produce testosterone. The testosterone is released by the testes and locks on to the androgen receptors located in the cells of the Wolffian ducts which stimulate it to form the male genital duct system.

The other hormone that is released by the testes is genetically encoded for on the 19^{th} chromosome and it produces what is called **Anti-Mullerian Hormone (AMH)**, also known as Mullerian Inhibiting Factor. But just like testosterone, it is incapable of causing an effect at the cellular level unless it locks on to a specific protein, which in this case is called the **AMH receptor**. The AMH receptor protein is genetically encoded for on the 12^{th} chromosome.

The release of AMH by the testes and its subsequent reaction with the AMH receptor located in the Mullerian duct cells causes them to degenerate, just like what would have happened to the Wolffian duct cells *without* the stimulation of testosterone. This is why the person who is an XY female because of CAIS does not have the internal female organs. Even though "her" testosterone is rendered incapable of stimulating the Wolffian ducts because of a defect in the androgen receptor, her Mullerian ducts also degenerate because of the effects of AMH produced in "her" testes.

Chopped Liver Dysfunction

But now let's look at what happens when there is a defect that results in the dysfunction of AMH or the AMH receptor in an XY male. This results in what is known as **Persistent Mullerian Duct Syndrome,** which if left uncorrected will result in sterility. In the situation where the Wolffian ducts do develop into the male genital duct system, but the Mullerian ducts persist and develop as well, they end up entrapping the testes preventing them from properly descending into the scrotum (crytporchidism) ultimately resulting in infertility. Nowadays, this defect is often surgically correctable but great care must be taken to preserve the vas deferens which is frequently embedded in the uterus and the fallopian tubes.

Last But Not Least

So far we've detailed how the SRY generates TDF which triggers the activity of, among other genes, DMRT-1, that goes on to stimulate the primordial undifferentiated gonads in the human embryo into becoming testes. These male testes then produce and secrete specific messenger hormone proteins called testosterone and AMH. The testosterone, by way of linking up with intracellular androgen receptors, goes on to trigger the Wolffian ducts into developing into the epididymis, the vas deferens, and the seminal vesicles; all of which are necessary for male reproductive function. Meanwhile, AMH attaches itself to a specific AMH receptor in the Mullerian duct cells and causes them to degenerate.

We've also seen that a defect of the androgen receptor, that is genetically encoded on the X chromosome, often will result in an XY person having ineffective testosterone which will result in the Wolffian ducts degenerating, making this person effectively sterile. In addition, if there is an isolated defect of AMH function, or the AMH receptor, then although the Wolffian ducts will develop properly, the resulting development of the Mullerian ducts will also render the XY male infertile due to having undescended testes.

But our understanding of adequate male reproductive function involves more than just having functioning testes, adequate testosterone and AMH secretion and properly functioning androgen receptors and AMH receptors resulting in Wolffian duct development and degeneration of the Mullerian ducts. We now need to address the development of the external genitalia. In the male we're talking about the penis, the scrotum, and the prostate; as opposed to the female clitoris, labia and lower vagina.

Remember, that the default sex of the human embryo is female. It requires enough androgenic stimulation to turn it from becoming a female to going down the road of becoming a male. The external genitalia develop from the (uro)genital sinus, swellings, folds, and tubercle, and they too must be acted upon by androgens in order to properly develop into the prostate, scrotum and penis. So one can see how an XY person with CAIS, although being absent the internal female genital ducts due to AMH, will have female external genitalia since their androgen receptors in these regions are defective as well.

One Final Twist

It has been shown that it is not testosterone per se, that is directly responsible for triggering the development of the male external genitalia. In fact it is a form of it called 5alpha-**dihydrotestosterone**, an hormone that comes about by the enzymatic action of 5alpha-reductase on testosterone. The androgen receptor is activated much more by dihydrotestosterone than testosterone itself, and this has been found to be vital for the development of the male external genitalia, and later in sexual maturation at puberty.

And as luck would have it, the tissue in the (uro)genital sinus and swellings, that are destined to become external genitalia, just happen to have the biochemical ability to convert testosterone into dihydrotestosterone. The Wolffian duct cells do not have this ability, but this does not prevent them from developing into the male internal duct system. So what do you think can happen when there's a deficiency or dysfunction of 5alpha-reductase, an enzyme that is known to be genetically encoded for on the #2 chromosome?

An XY person who has 5alpha reductase deficiency, a rare autosomal recessive disorder, will have normally functioning testes, each with a normal epididymis, vas deferens, and seminal vesicle. However, their external genitalia will be markedly deformed making them incapable of proper sexual intercourse, and usually ambiguous with regard to whether they are male or female. If considered male: they will be at least impotent, and if seen as being female: they will be sterile, a situation that nonetheless would prevent them from passing on their genes to the next generation.

Summary and Questions for Macroevolution

The ability for humans to be able to reproduce is dependent on having a male and female of the species. It has been clearly demonstrated that the human embryo by default is destined to become female unless it is acted upon by several biomolecules acting together through specific receptors contained in the primordial undifferentiated cells that are to become the male reproductive system. At a minimum, the absence of any one of these proteins; such as the TDF, DMRT-1, testosterone and each of the multiple enzymes necessary for its formation, the androgen receptor, AMH and the AMH receptor, and 5alpha-reductase, results in the development of either a female phenotype, or a male that is impotent and infertile. Either way, reproduction as we know it, resulting in the continuation of any species leading up to homo sapiens, would be physically impossible and the idea that only natural selection acting on random variation could explain human evolution would literally be dead.

If I were a student of Science and were aware of all of what has been placed here before me, I would have several questions that need answers from the Darwinists of our time before I would be convinced of the truthfulness of their theory. Here's a few of them.

- Rather than just noting that other more primitive organisms have similar embryonic structures as precursors for similar reproductive systems, please explain; how these more primitive structures came into being in the first place; what additional genetic changes must have taken place to allow for this development; and where did this new genetic material come from ? Be specific as to how these complicated tissues came into being through the formation and organization of very complex macromolecules.
- Even though it is evident that similar organisms use similar trigger mechanisms, such as DMRT-1, to differentiate

primordial tissue into the male line, how did this come about, and given the fact that there are many other different factors required, most of which have yet to be determined, how can one be so certain, scientifically, that they came about by the random forces of nature, when it is evident that all of them are needed for proper function? How did each system work every step along the way without what we know to be the necessary proteins that are needed for this function?

- There are many enzymes that are encoded on many different chromosomes that are necessary for adequate testosterone production, and it has been demonstrated that absent the proper function of any one of these, that male reproduction is impossible. How then could such a system have developed while remaining functional to allow for the propagation and transmission of genetic material to subsequent generations?
- Both testosterone and dihydrotestosterone are vital for the development of a human male that is capable of reproduction. But their ability to accomplish this is dependent on the presence of both, a properly functioning androgen receptor, and the enzyme 5alpha- reductase. How could the continued survival of each progenitor of the hominid species have taken place without the present system and describe how each innovation was incorporated into an intermediate primordial one.
- AMH and the AMH receptor are vital for the proper development of a human male that is capable of reproduction. How were these proteins incorporated over time into what is presently understood as the process of male sexual development of the human embryo? How did the prior system(s) function without either, or both, of these proteins, to allow for adequate fertility?

It is my contention that the evidence put forth by Darwinists to "prove" macroevolution; that the complexity and diversity of all life has come about entirely by the random forces of nature without an intelligent agent at work; is at best, *circumstantial*. They have simply seen similar structures within various organisms of differing complexity and have concluded that because reproduction takes place that this is sufficient to explain their development over time. Along the way, except to those who, a priori, accept, or must accept, Darwinism as dogma, they have, in my opinion, neglected to sufficiently explain;

- the organization of mere chemicals into DNA and a complex functioning cell,
- the organization of cells into a multi-system organism with a complex body plan, and,
- the fact that the biomolecular basis of life, as just one example of thousands or more demonstrated here, is dependent on irreducibly complex systems each consisting of numerous specific proteins, acting on specific cells, by way of specific receptors

No one refutes that natural selection acting on random variation does have an effect on species development. But, based on what we know about how life works, and more importantly, how easy it is for disease, dysfunction, and death to muck up the works, is it even reasonable to assume what Darwinists foist upon the public?

As best expressed by Dr. Wm Dembski: "The central claim of evolutionary biology is that an unguided physical process is sufficient to account for the emergence of biological complexity and diversity." "Intelligent design" as per Dr. Dembski, "is the science that studies signs of intelligence. Note that a sign is not the thing signified. Intelligent Design does not try to get into the mind of a designer and figure out what a designer is thinking. Its focus is not designer's mind but the artifact."

If you were walking down a deserted beach and suddenly saw the letters H-E-L-P etched in the sand, is it likely that you would think it came about solely by the random forces of nature? No, and if you didn't bother looking around to see who needed help I think that an alibi based on your conclusion that this was not a "mind" at work, a "mind" that needed assistance, would make you at best, look the fool, and at worst, a pariah.

But if you found the letters H-L-E-P instead: would you now be more inclined to think that this could not have been the work of intelligent design, because although you could figure out what it probably meant, it wasn't arranged in a way that you thought was proper? I doubt it. For if the person making the marks were expressing themselves in an unknown language or code, you would not be able to discern the correctness of the message, but your intellect would alert you to the fact that a "mind" was indeed at work.

This is one of the arguments put forth by many Darwinists to try to refute intelligent design. In essence they are saying that life could not have had any intelligent agent involved in its development because it didn't come about the way they would have done it, or it's not what they would have expected.

When we decide that something likely has had an intelligence involved in its making, a mind at work, we recognize something that to us has meaning, function, or aesthetic value, such as a message, a machine, or a beautiful painting. And that this could only exist by something or someone having chosen this particular pattern over a multitude of possibilities: like the imposition of the letters H-E-L-P, or the parts of a car, or the oil pigments on canvas. So when we distinguish

between naturally occurring events and intelligently caused ones we do it by using our minds to detect some sort of information, pattern, useful function, or design, that means something to us.

You see, it takes one to know one. You have to have an intellect to be able to detect intelligent design. But we and our children are supposed to believe this paradox spun out by evolutionary biologists. That the very intellect that each of us possesses, which gives us the capacity to detect intelligence, came about by the unguided random forces of nature; forces that all experience tells us can't produce anything that is considered intellectually significant.

Ideas have consequences. We all are human and have philosophical and ideological models that we follow in life. Scientists who continue to expound dogmatically on the truth of macroevolution, without at least admitting to the weaknesses of their claims, while showing no appreciation for its effects on our culture, at best, are ignorant of the human heart and mind, and at worst, are being disingenuous and intellectually dishonest.

Next Time

Now that you know how the male genital system comes into being, next time we'll take a look at how a properly outfitted man is able to perform his part of human reproduction.

Join us then for: Male Sexual Function: (How Exactly Does Viagra Work?)

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