Throughout our bodies, thousands of genes act differently in men and women

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Most of us are familiar with the genetic differences between men and women.

Men have X and Y sex chromosomes, and women have two X chromosomes. We know that genes on these chromosomes may act

differently in men and women.

But a recent paper claims that beyond just genes on X and Y, a full third of our genome is behaving very differently in men and women.

These new data pose challenges for science, medicine and maybe even gender equity.

The human genome

Men and women have practically the same set of about 20,000 genes. The only physical difference in their genetic make up is in the sex chromosomes. Only males have a Y chromosome. Although the X chromosome is present in both sexes, there are two copies in females and only one in males.

The human Y contains only 27 genes. One of these is the sex-determining region Y gene (SRY), which kick-starts the pathway that causes a ridge of cells in a 12 week-old embryo to develop into a testis.

Until recently, many believed that only the presence or absence of SRY distinguishes men and women.

Writing previously, I pointed out that there are 26 other genes on the Y chromosome, and perhaps another hundred or so genes on the X chromosome that are active in two doses in women and a single dose in men. I speculated that there may be a few hundred more genes directly affected by these X or Y genes, or by the hormones that they unleash.

This new paper suggests I underestimated by a huge margin.

Genes, proteins and tissues

Genes are parts of a long string of DNA, and composed of molecules that contain four different bases. The sequences of these bases encode the proteins of the body.

Our 20,000 genes make proteins that do a variety of jobs. Some make the fibres in skin or hair, some make muscles contract, and others carry the oxygen in blood. Many are enzymes that drive basic reactions of turning food into flesh and energy.

Genes work by making copies of themselves; the base sequence of DNA is copied into RNA molecules that engage with cell machinery to churn out protein. The more RNA a gene makes, the more protein will be produced.

We can now measure the number of RNA copies each gene makes. A really active gene may make thousands of copies, an inactive gene may make only a few, or none at all.

This epigenetic ("over the gene") regulation of gene activity allows specialisation of different body tissues. Your liver and your brain share the same genes, but express them differently; one subset of genes is active in the liver, and a different subset of genes is active in the brain.

Activity of genes in men and women

In their new paper, the authors Gershoni and Pietrokovsk looked at how active the same genes are in men and women. They measured the RNA produced by 18,670 genes in 53 different tissues (45 common to both sexes) in 544 adult post mortem donors (357 men and 187 women).

They found that about one third of these genes (more than 6,500) had very different activities in men and women. Some genes were active in men only or women only. Many genes were far more active in one sex or

the other.

A few of these genes showed sex biased activity in every tissue of the body. More commonly, the difference was seen in one or a few tissues.

Most of these genes were not on sex chromosomes: only a few lay on the Y or the X.

How could a third of our genes be differently controlled in men and women?

We now understand that proteins work in extensive networks. Change the amount of one protein produced by one gene, and you change the amounts of all the proteins produced by many genes in a long chain of command.

We also know that hormones have powerful influences on gene activity. For instance, testosterone and estrogen dial up or down many genes in reproductive and body tissues.

Impact on physical features

The functions of sex biased genes makes some sense. Most affect the reproductive system, which we know to be very different in men and women. For instance, the new study shows that mammary glands have highest frequency of female-biased gene expression, and testis has the highest frequency of male-biased genes.

Other sex biased genes were involved with skin (particular hairiness), muscle, fat tissue and heart, which could relate to sex differences in body morphology and metabolism.

Confirming an earlier report, some sex biased genes were involved in

brain function, reopening the debate about differences in male and female behaviour.

Impact on disease susceptibility

These new findings could explain why men and women are often differently susceptible to diseases, and suggests treatments need to be based on studies of both sexes.

We have long known that many diseases are far more common in men (e.g. Parkinsons) or in women (e.g. Multiple Sclerosis).

This study showed that some sex-biased genes were associated with diseases. For instance, a female-biased gene is implicated in cardiovascular homeostasis and osteoporosis, and a male-biased gene in high blood pressure.

The new study also showed a big difference in expression of a gene previously found to be important for drug metabolism, which could explain why men and women may respond quite differently.

The Organization for the Study of Sex Differences has campaigned to include women in clinical trials. These results should strengthen their hand.

Like it or not, evidence now shows that men and women differ genetically far more profoundly that we have previously recognised.

What do these new insights mean for our progress toward gender equity? A bad outcome could be appeals to return to outdated sexual stereotypes. A good outcome will be recognition of sex differences in medicine and treatment.