**Brand new research - NOT peer-reviewed yet, a few take-aways**

# MAREK'S DISEASE

## GIRLS IN TROUBLE

*Sex differences in response to Marek's Disease*

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**Hens are more vulnerable: FACT.**
**Because of the higher susceptibility of hens to Marek's Disease the Z-chromosome was investigated for possible clues on 'why'.**
**The chickens used were made for other research and are layers (Hy-line) and eight other commercial layer lines.**

**The problem is localising where the genes are which influence tolerance of MD.** There are already regions known, here they look beyond the known regions and took larger parts of the genome. Since the Z chromosome is unique to hens (otherwise they weren't hens) they looked for genes that might play a role in susceptibility to MD.

**In general, most females have a better immune system to infections compared to males and cope better and have less severe symptoms.** In birds however, who need a mum and a dad too, the females are heterogametic (heterozygous or also called hemizygous sex chromosomes, half a pair (Z/W) the W stands for nothing which I write as Z/-) and males are homogametic (Z/Z). In mammals it is the other way around.

For chickens we know the result of this, only dads give sex-linked traits to their daughters. The daughters show this regardless whether a dominant or a recessive sex-linked gene, for example gold and silver. When dad is homozygous gold (s+/s+), all daughters are gold (s+/-), regardless of what the mother is. Mum does give her s+ or S to her sons, next to dad. Therefore hens are either gold or silver and sons can be both (s+/s+ when mum is gold too, S/s+ when mum is silver).

W or /- although everywhere present in female tissues, contains mainly housekeeping genes which don't specifically serve female beneficient functions. On this bird /W I attached the title of a specific research paper if you are interested. The other allele Z 'our' sex-linked part is functional for the obvious sex-differences and during evolution it had to be balanced for the autosomal genes (functional in

both sexes) to prevent it would not run things into the soup for the opposing sex.

This preventive measure, to not screw things up for the other sex, is called 'dosage compensation'.
It has to do with the expression of genes on the sex chromosome. This makes sense, right?

**Now, here it comes. This system of dosage compensation is not present in chickens.**
It is most frequently seen in XY mammals (males). In chickens the genes on female Z/W are totally different from the genes on male Z/Z. They are much better organised compared to mammals and plants for that matter. This whole dosage compensation thing is not necessary in chickens. More need to be explored on this. Science is looking into genes on W and also pseudo-autosomal genes located there. It is not yet exactly known which and where pseudo-autosomal genes can be found in W. Anyway, they are working on it.

**On Marek's Disease (MD).**
**A costly disease, both in lives and costs of vaccinations.** This herpes family virus suppresses the immune system, it causes cancer, depression and paralysis because the nervous system is attacked. Chickens lose appetite, get diarrhoe and therefore weight. They can get anemia and can become dehydrated. Mortality is high and surviving chickens might get other (secondary) infections because the T-cells are attacked. You know all this already.

**Who is more susceptible to MD, cocks or hens?** There were several studies on this and the opinions differed. Hormones (testosterone and oestrogen) were mentioned as having influence on immune responses. How different immune cells mature, how fast, how long they live, is different in male and female birds.
Susceptibility to infection is higher in heterogametic individuals (XY mammal males and ZW female birds) from birth throughout adulthood till they drop.
**Where human females live longer to the dread of (some) male humans, male birds tend to live longer than females.** This might subconsciously explain cocky behaviour in male humans? Cocky behaviour might not help human males much, since chicken cocks live only 7.1% longer than hens. Not enough to plan life's winter. Human females live 20.9% longer than males, therefore they are the strong, most durable sex.

**This Z/W and X/Y difference is called in mammals 'the unguarded X' hypothesis.** It suggests that the absent part of the sex chromosome, exposes bad recessive mutations on the other one. This suggests that sex chromosomes have a major role in immune response, more so than hormones.

**Immunity by birth (innate immunity) is the first line of defence and contributes to the adaptive (acquired) immune response throughout life.** In mammals innate immune molecules are on the X chromosome, with different consequences of their expression in either sex. In chickens, several genes are involved on the Z chromosome.

**Vaccination against MD prevents tumours, but doesn't prevent infection or shedding of the virus although less.** Therefore MD is still found in vaccinated chickens, and this can give rise to more virulent MD variants. If so, vaccines become less effective. A way to tackle this, is improving the innate immunity of chickens.

**SvD: plenty breeders do not vaccinate against MD, their chickens are mostly immune.**
Industry is doing the same, there are several commercial chicken populations which show a much better resistance against MD. There are more animals and plants bred for disease resistance. The problem is that the genetic value overall, dropped by 40% in the long term, due to loss of useful genes. This looks like putting the cart before the horse. Now they try to pinpoint exactly what genes are responsible for a better immune response to prevent the loss of other valuable genes. To do this, they use QTL mapping. QTLs are places on the genome (dna) where traits are located. Scientists are searching for decades where exactly the 'anti MD genes' are located. They had limited success. There are many places contributing to innate immunity and only the sum of all, achieves this. They lay scattered allover the place. One place was identified for sure regarding disease resistance including MD (https://pubmed.ncbi.nlm.nih.gov/33147703/) if you want to know more.

**Because hens are more susceptible, they looked for possible genes or QTLs on the Z/- chromosome.** In order not to annoy you with how they did it, which I don't fully understand anyway, here the conclusion. Note that this paper has yet to be peer-reviewed, others 'who know' are going to look into the data, so nothing is guaranteed yet.

**The conclusion: they DID find regions on the chromosome with candidate genes that might explain part of the gender difference in immune response to MD.**
However all the anti-MD-genes are scattered as said before for as far as they are reported. The additional problem is that the resistance to MD differs per line and even per MD variety. This means that only tailor made breeding should work and MD should not mutate and undo all the careful breeding up. Suggested is therefore, to edit the found genes in immune chickens, which will give a better insight in how they contribute to viral immunity. Editing means: isolate the immune-gene and put it into a chicken, without the lengthly process of breeding. You get the first 'adjusted' chickens in the next year instead of 10 or even 50 years later because all the existing traits (laying, meat) stay intact.

Gene editing of chickens, the benefits. Read my article (Dec. 2022) on the website www.chickencolours.com > Articles, scroll down till you find it.

2022 The new paper: https://www.preprints.org/manuscript/202212.0025/v1
2020 The Female-Specific W Chromosomes of Birds Have Conserved Gene Contents but Are Not Feminized