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# Sex and Gender dimension in frontier research
# ERC annual conference

## SESSION 1 - Gender in medicine and medical care - Q&A

**Q1: having SABV as a basis, 1) Controlling/adjusting by the variable sex could be consider contradictory, since we are removing the effect of sex on the outcome variable. 2) If data are not disaggregated would you suggest to always test the interaction in between sex and the predictor variable?**

**Natasha KARP reply :** When you design an experiment to include sex in addition to a second variable of interest (e.g. treatment) you are moving from a randomised complete design to a factorial design. In a factorial design you use statistical methods such as regression or a two-way ANVOA which enable you to test the effect of sex, the effect of treatment and whether the effect of treatment depends on sex. In these approaches, you are estimating the effect of treatment after accounting for a potential effect of sex, this actually can increase sensitivity as any difference that is just due to sex of the animals or cells is accounted for.
If you have collected data on both sexes at the same time, then you now have the potential to statistically test whether the treatment effect depends on sex. This gives you additional biological insight. These factorial designs are recommended as they are more efficient and allow you to understand the biology in a more nuanced manner. This can be compared to the option of collecting the data on both sexes in two separate experiments. When you run independent experiments, you needs more animals as each experiment has to be powered separately and you do not share information. Furthermore you cannot explore whether any differences seen in treatment effect is due to the fact it was run on different days or was due to the effect of sex.

**Q2 : In general, female populations have a lesser cancer susceptibility than male populations. Is the reverse true in Drosophila, or does it apply only to the system you are studying ?**

**Irene Miguel Aliaga reply** : It depends on what tumours in Drosophila. Whilst female guts are more susceptible to genetically induced tumours, other tumours (e.g. certain brain tumours) are more invasive and malignant in males – see , for example. Alos, whilst it is true that, overall, (human) females are less susceptible to cancer, this is also cancer dependent and in some case it is the other way around. Susceptibility is likely to be influenced by multiple factors (diet, lifestyles, genetics including sex chromosomes and sex hormones); the relative contribution remains to be established in many cases.

**Q3: Irene for a very interesting talk! Until now I thought that in Drosophila sex was entirely genetically determined at a single-cell level, but you seem to suggest that there is some hormone-like system on top of that. Could you please elaborate on that, and the relative prevalence/importance of each mechanism? A more concrete question would be: having single-cell sex determination would mean that in an overall female individual just by chance we might observe some "male cells". Is this what we'd expect or is there a mechanism regulating that? Many thanks in advance.**

**Irene Miguel Aliaga reply** : Thank you! Yes this is changing. Both our work and that of others (e.g. Rideout, Edgar labs) has recently provided evidence for extrinsic contributions in flies. In parallel, the mammalian field is beginning to acknowledge contributions of intrinsic mechanisms to sex differences in physiology (Karen Reue and Art Arnold have written about it).

The plasticity of sexual fate is a very interesting question and there is of course evidence for it in other species (e.g. fish). But how plastic is the sexual fate of specific cells and/or organ within a male or a female is something we have not explored yet in flies but we would like to do so.

**Q4: Do you think that we should consider then increase awareness for colon cancer screening not only in men but also women?**

**Irene Miguel Aliaga reply** : I would not extrapolate that far from our work in flies! I think what our work with stem cells and tumours say is that possible contributions of "cell-intrinsic sex" are worth considering in the context of cancer.

**Q5: Could this mean that one should pay attention when it comes to organ transplants and make sure they are only transplanted between people of the same gender?**

**Irene Miguel Aliaga reply** : I have not looked at this literature in detail so I am not sure how systematically this has been tested but there is some experimental work in mice that suggests that the sex of transplanted cells can impact the outcome of the transplantation experiment.

**Q6: As we share so many genes in common - what do you think is driving the differences in expression levels? For me, this raises questions about evolution how would these sex differences be optimised differences?**

**Irene Miguel Aliaga reply** : Some of the sex differences will indeed be species specific, given that the sex-specific needs of species are likely to differ (e.g. reproductive, nutritional). The value of studying them in flies is in uncovering how these sex differences arise and why they matter; this provides a conceptual framework to think about our own sex-biased (patho) physiology and its implications.

**Q7: Determination would mean that in an overall female individual just by chance we might observe some "male cells". Is this what we'd expect or is there a mechanism regulating that?**

**Irene Miguel Aliaga reply** : Not necessarily; you could argue that by having different ways to specify sexual fate you make this fate more robust. Alternatively, they may all be differentially affected by

factors such as internal state, nutrient availability, etc to differentially modulate the sexual fate of specific cells or organs (i.e. make them “more” or “less” female).

**Q8: From your gene expression studies, Do you identify genes in particular pathways or throughout the genome**

**Irene Miguel Aliaga reply** : Throughout the genome; we describe all the genes that are active (namely, making a transcript) by a particular cell or organ at a specific time.

**Q9: Is it depending gut proliferation during the pregnancy if you carry male or female sex?**

**Irene Miguel Aliaga reply** : If you mean fly “pregnancy” the answer is yes; the stem cells of females need to be female to be able to proliferate more and resize the gut during reproduction. In humans we don’t know.

**Q10:**

Irene's talk reminded me of Crohn's Disease and Inflammatory Bowel Disease in general. A quick search yielded this recent review that may serve as a complementary reading, and a case directly applied to a human disease, for all interested:

"Gender Differences in Inflammatory Bowel Disease"

Digestion 2020;101(suppl 1):98–104

https://www.karger.com/Article/Fulltext/504701

Free Access

Perhaps Irene's research can find a parallel here?

**Irene Miguel Aliaga reply** : Thanks! Yes, several aspects of many GI disorders (e.g. Hirschsprung's, gastroparesis, IBD) are sex-biased and/or modulated by reproduction for reasons