

## Propositions belonging to this thesis

1. X-encoded activators are differentially expressed between the sexes, allowing a cell to count the number of active X chromosomes. Autosomally encoded *Xist* activators are equally expressed in males and females and merely put pressure on the threshold for XCI to occur. (this thesis)
2. UBA1 is an X-encoded XCI activator and most likely functions in a cascade to activate XCI. (this thesis)
3. *Rnf6* is an *Xist* activator and functions in XCI through down regulation of REX1. (this thesis)
4. The Xi established by imprinted or random XCI do not differ with regard to chromatin marks. The difference in stability more likely depends on DNA methylation. (this thesis)
5. Semi-stable transcriptional states of *Xist* and *Tsix* represent distinct states of transcriptional activity and likely plays a role in epigenetic memory. (this thesis)
6. In *in vivo* knockout studies are essential for deciphering biological processes, including XCI. However, careful consideration should be taken with regard to the timing of expression of the Sox2Cre transgene to conditionally delete *Xist* or *Rnf12* in the post-implantation epiblast, which possibly occurs after the window of opportunity of XCI. (Shin et al., 2014. *Nature* 511, 86-89; Minocha et al., 2016. *Dev Biol* 418, 75-88; Yang et al., 2016. *Genes Dev* 30, 1747-1760)
7. Negative results showing no improvement, no effect or the unexpected are still important findings. Lack of sharing such results simply results in skewed literature and allows everyone to make the same “mistakes”.
8. “The success of CRISPR/Cas9 highlights another general tenet of science: basic, fundamental research can lead to transformative discoveries” (Feng Zhang).
9. “Medicine, the only profession that labors incessantly to destroy the reason for its existence.” (James Bryce)
10. Natural biological systems, due to their large diversity, redundancy and robustness, are often difficult to explain and recapitulate with simplified man-made systems and standardized models.
11. Science is never black or white, but rather fifty shades of grey.

Cheryl Mandy Maduro