Placental phenotype differences between XmO and XpO in Turner Syndrome

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Objective
Turner syndrome arises from the loss of genetic material from one of the sex chromosomes resulting in the 45 XO genotype with the remaining X chromosome being maternally-inherited (Xm) or paternally-inherited (Xp). As the gene dosage and expressions of the Xp and Xm chromosomes may not be equivalent epigenetically. The aim of this study is to investigate different influences of Xm and Xp on placental phenotype using a mouse model.

Methods
14 placentas from pre-term MF1 mice (3XX, 3XY, 5XmO, 3XpO) at 18. 5 days post-coitum were isolated, formalin-fixed, paraffin-embedded and sectioned. To examine the morphological differences between the four placenta types, sections were stained histologically (H&E, PAS, Heidenhain’s Azan) and immunohistochemically (for CDX2, CK19, fibronectin, laminin, pcam-1). Student’s t-test was used to statistically analyse the different comparison parameters such as the size of the placenta, layers, cell density, CDX2-positive and glycogen cell numbers in the junctional zone (Jz).

Results
Wild-type (XX, XY) placentas are quite similar to each other. XpO placentas are significantly different from the other three genotypes, especially in the Jz being thicker especially at the lateral end of the placenta (p=0. 038). Moreover, the numbers of CDX2-positive (p=0. 0092) and glycogen cells (p=0. 017) are increased. XmO placentas exhibit large morphological variations as some were phenotypically similar to wild-type placentas while others were phenotypically similar to XpO placentas. Some XmO placentas (n=3) also have a 15° upward tilt at the lateral end not observed in the other genotypes.

Conclusion
Xm and Xp affect placental development differently. Xp is normally silenced in the extraembryonic tissues of the murine placenta, if it is activated in the absence of a second sex chromosome it will result in a placenta morphologically different from normal. Conversely, XmO placentas look phenotypically more normal, although, they also exhibit some defects suggesting that Xm alone is insufficient to form a normal placenta. Our findings are consistent with literature stating that XpO fetuses are less viable than XmO fetuses, since we found that XpO placentas exhibit the largest degree of phenotypical abnormality while XmO placentas share mixed characteristics between the wild-type and XpO placentas. XmO placentas may function better than XpO placentas resulting in a viable pregnancy. This is also consistent with literature which documented that most of the human 45, XO fetuses that survive to birth have Xm.