

MOLECULAR STUDY OF THE ENDOMETRIAL IMPACT AFTER SURGICAL RESECTION IN DEEP ENDOMETRIOSIS

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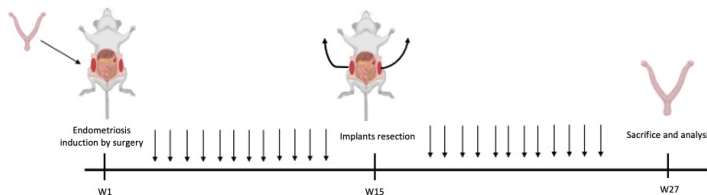
CONTEXT

The question of the existence of an intrinsic abnormality of the endometrium or one induced by presence of endometriosis remain unclear. In presence of endometriosis, eutopic endometrium is known to harbor molecular alterations. A positive impact of surgical resection of deep endometriosis lesions on endometrial function remain questioned. Surgery could interrupt an inflammatory dialogue between ectopic lesions and eutopic endometrium.

OBJECTIVE

The objective is to determine, in a mouse model of endometriosis, if resection of lesions can restore gene expression profile of eutopic endometrium.

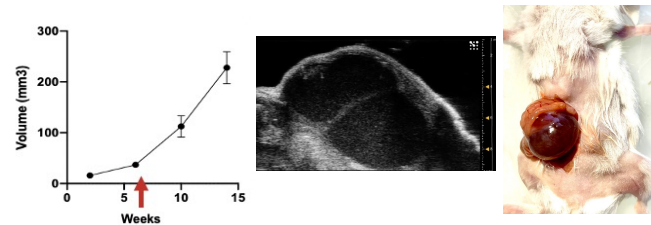
MATERIAL & METHODS



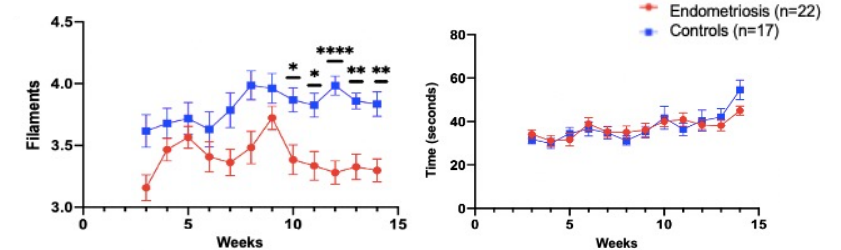
BalB/c mouse model of endometriosis was performed by grafting bilateral uterine horn implants from BalB/c donor. Implants were resected at 15 weeks; sham laparotomy was performed for controls. Sacrifice occurs at 15 weeks of resection of lesions and comparative RNAseq transcriptomic analysis of uterine horns was conducted between resected, implanted and control groups.

RESULTS

Implants growth



Behavioral nociception tests

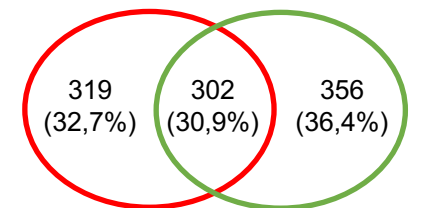


The size of implants increased after **6 weeks** in association with a **decrease in the nociception threshold in Von Frey test**, but no difference in hot plate test or behavior in new object recognition.

Comparaison of the endometrial transcriptome

Of the 621 genes deregulated in the eutopic endometrium in presence of endometriosis, **surgery restored an expression profile comparable to controls for 319 genes**. Almost half of these genes were down regulated, and their expression profile shows a significant enrichment of pathways involved in **innate or adaptative immunity**. Other changes in the expression profile were not reversible by surgery, such as metabolic retinol pathway.

Endometriosis vs controls (red circle)
Endometriosis resection vs controls (green circle)



CONCLUSION

Surgical resection of implants in a mouse model long exposition to endometriosis has an impact on endometrial gene expression. These results are to be confirmed, they could possibly help us to define therapeutic targets in the objective of improving spontaneous fertility and pregnancy issues.

References

¹Chapron C, Marcellin L, Borghese B, Santulli P. Rethinking mechanisms, diagnosis and management of endometriosis. Nat Rev Endocrinol. 2019;15(11):666–82.

²Symons LK, Miller JE, Kay VR, Marks RM, Liblik K, Koti M, et al. The Immunopathophysiology of Endometriosis. Trends Mol Med. 2018 Sep;24(9):748–62.

³Liu H, Lang JH. Is abnormal eutopic endometrium the cause of endometriosis? The role of eutopic endometrium in pathogenesis of endometriosis. Med Sci Monit Int Med J Exp Clin Res. 2011 Apr;17(4):RA92-99.

⁴Le NXH, Loret de Mola JR, Bremer P, Groesch K, Wilson T, Diaz-Sylvester P, et al. Alteration of systemic and uterine endometrial immune populations in patients with endometriosis. Am J Reprod Immunol. 2021 Mar.