

Loss of epithelial Jagged 1 disrupts the integrity of adult homeostatic mammary gland

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INTRODUCTION

- Adult mammary gland is composed by a branching epithelium that fills the stroma or mesenchyme also known as mammary fat pad.

- Notch signaling is a master regulator of cell fate choices during development and regeneration of several tissues including mammary gland.

- Epithelial deletion of the Notch signaling ligand Jagged1 in K14CreJag1fl/fl mice results in the development of mammary tumors in females around 8-12 months-old.

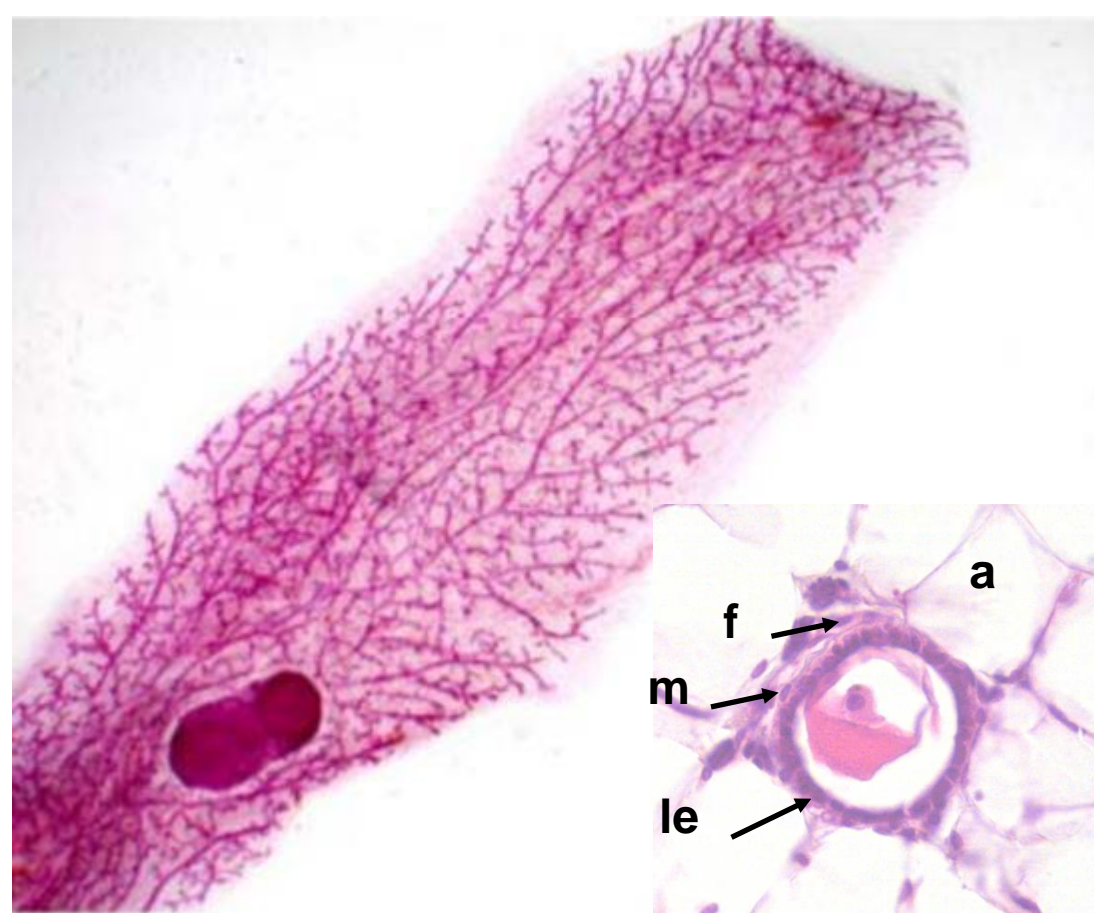


Figure 1. Carmin alum stained adult mouse mammary gland showing the branching epithelium filling the fat pad. Inset: Hematoxylin-eosin stained cross-section of a mammary duct. Abbreviations: a, adipocytes; f, fibroblast; le, luminal epithelium; m, myoepithelium.

RESULTS

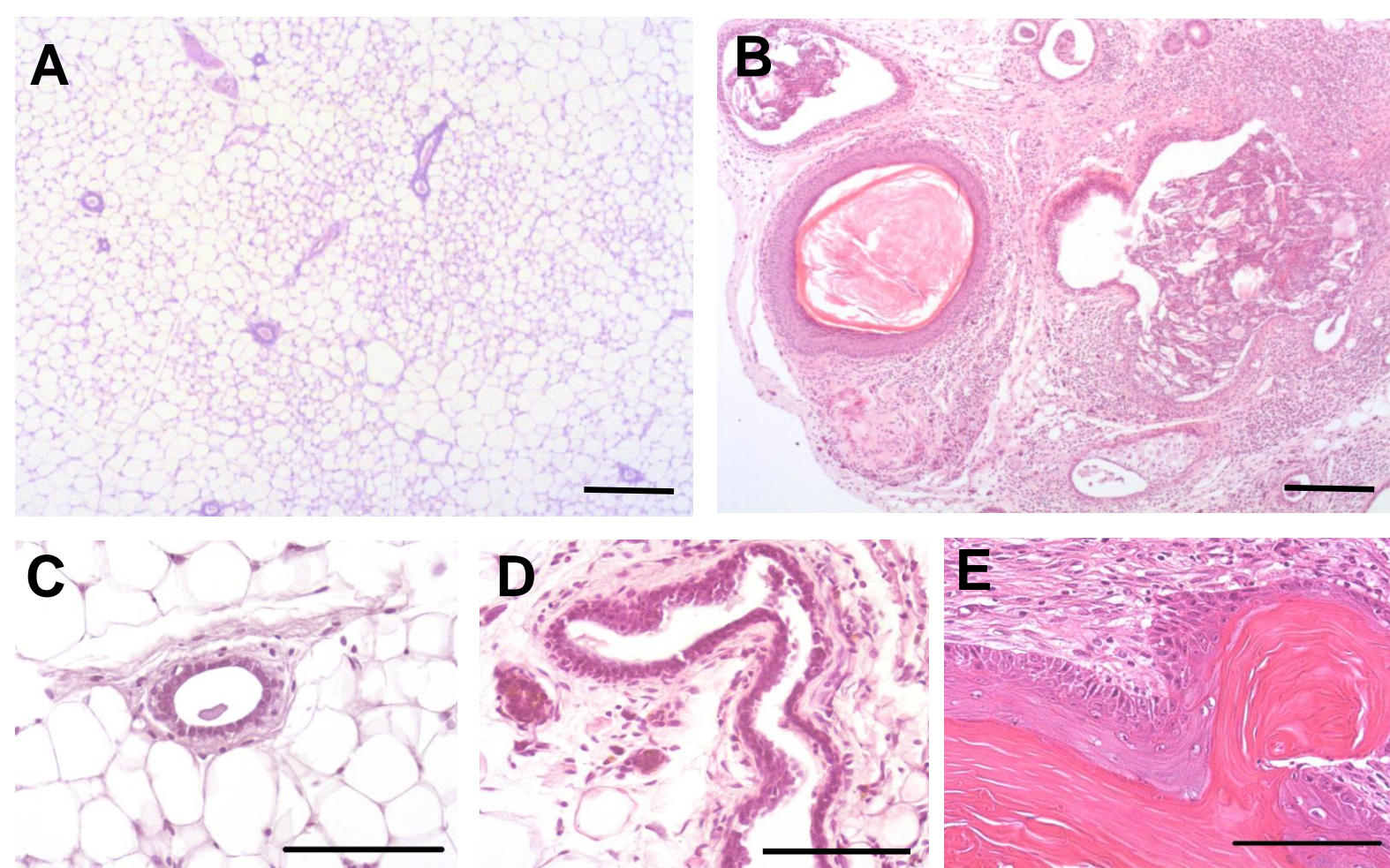


Figure 2. Hematoxylin-eosin staining of control (A, C) and K14CreJag1fl/fl mammary glands (B, D, E) showing the presence of distended ducts and epidermoid cysts in K14CreJag1fl/fl mammary glands. Scale bars: 300µm (A, B), 100µm (C, D, E).

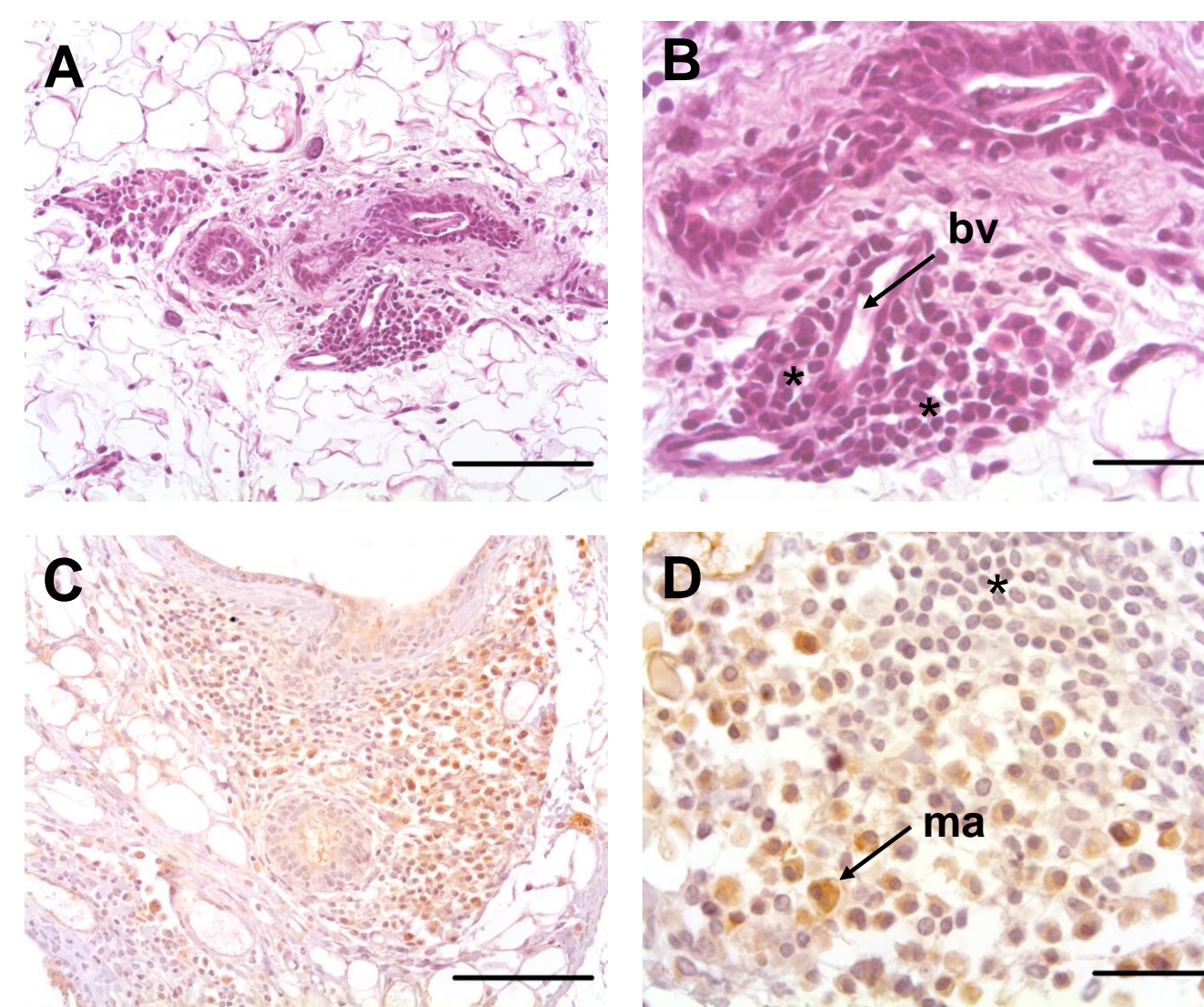


Figure 2. Hematoxylin-eosin staining (A, B) and CD68 immunohistochemistry (C, D) showing infiltration of immune cells in K14CreJag1fl/fl mammary stroma. Abbreviations: bv, blood vessel; ma, macrophage. Asterisks mark infiltrating leucocytes. Scale bars: 300µm (A, C), 100µm (B, D).

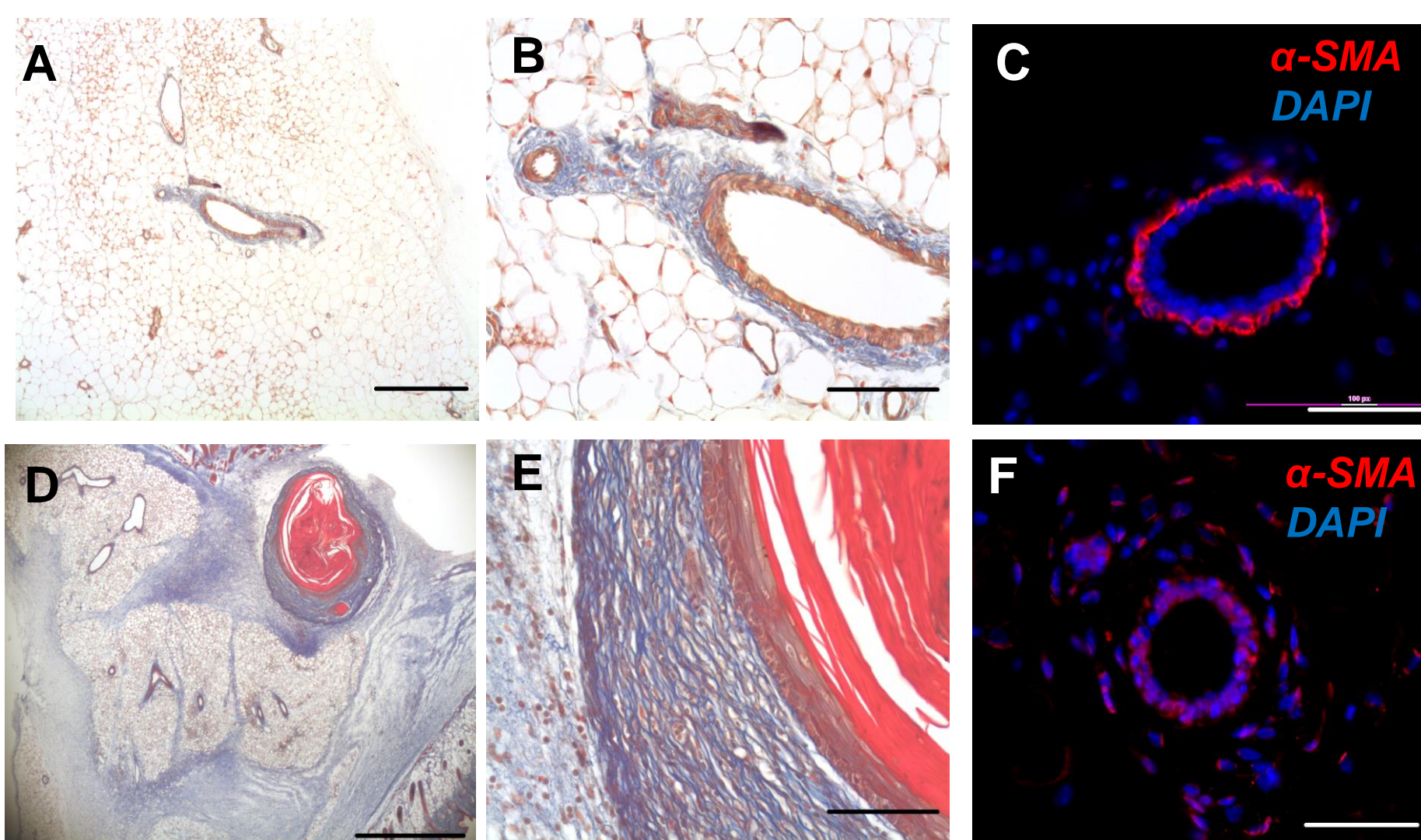


Figure 3. Masson's trichrome staining of control (A, B) and K14CreJag1fl/fl (D, E) mammary glands showing fibrosis (increased amount of blue collagen fibers) in mammary stroma and around epidermoid cysts developed in K14CreJag1fl/fl mice.

Immunofluorescence staining against α-SMA showing myofibroblasts in periductal stroma in K14CreJag1fl/fl mice. α-SMA is expressed by myoepithelial epithelium in control duct (C) whereas presents an aberrant expression in K14CreJag1fl/fl epithelium (F). Scale bars: 375 µm (A, D), 100µm (B, E), 50µm (C, F).

SUMMARY

- We have observed the presence of epidermoid cysts, distended epithelial ducts, and abnormal expression of some lineage-specific markers suggesting that Jagged1-depleted mammary epithelium undergoes transdifferentiation and/or dedifferentiation events.
- Mammary stroma also appears altered in K14CreJag1fl/fl mice, showing infiltration of immune cells as well as fibrosis.
- In conclusion, our results reveal a crucial role for epithelial Jagged1 in the maintenance of the integrity of adult mammary glands.

ACKNOWLEDGEMENTS

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