

# Secretory Leukocyte Protease Inhibitor: Immunohistochemical Evidence Supporting a Fallopian Tube Origin for Serous Papillary Carcinoma

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## Introduction

Serous papillary carcinoma (SPC) represents the most common histological type of ovarian carcinoma, which is the fifth leading cause of cancer-related death in women in the United States.<sup>1</sup> The tissue of origin for SPC remains controversial. It is believed by many authors that the cancer arises from the surface epithelia of the ovary or the cells that line ovarian inclusion cysts.<sup>2,3</sup> In this theory, the ovarian surface epithelium (OSE), usually flattened with no distinct features, undergoes Mullerian metaplasia and through possible undefined molecular events, acquires serous papillary morphology during malignant transformation. A contrasting opinion is that SPC may arise from the fallopian tube (FT), this supposition based on the morphologic resemblance of SPC to the fimbriated end of the FT. A recent report<sup>4</sup> investigating the patterns of gene expression among different histotypes of epithelial ovarian cancer showed strong correlation of expression profile of serous papillary carcinoma with that of the fallopian tube.

Protein expression profiling by immunohistochemistry provides a straightforward method to delineate the tissue origin of cancer cells, and is the basis for panels of antibodies used in the work up of tumors of unknown origin. The differential expression of proteins can similarly be exploited to help establish the origin of tumors of ambiguous origin. Proteins expressed in non-malignant cells may continue to be expressed in their malignant counterparts. Thus, cell lineage can be extrapolated by examining protein expression in non-malignant cells (e.g., FT or OSE) and their purported malignant counterpart (SPC). We have used this strategy with an antibody to Secretory Leukocyte Protease Inhibitor (SLPI), a 12-kDa protein found in various fluids including parotid secretions, cervical mucus, seminal plasma, ascites, and amniotic fluid. A potent inhibitor of human leukocyte elastase, SLPI is also shown to inhibit cathepsin G and trypsin. Previously it had been demonstrated that SLPI is expressed in FT tissue by Western blot analysis, RT-PCR and immunohistochemistry.<sup>4</sup> The aim of this study was to further characterize the expression of SLPI and examine its utility in the assessment of the cell lineage for SPC.

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## Experimental design and methods

Nine separate cases of formalin fixed, paraffin embedded tissue blocks containing the fimbriated end of the FT, nine cases of ovarian tissue with intact OSE, and nine cases of ovarian SPC were selected from the archival files of the Department of Pathology.

Slides were prepared using standard antigen retrieval techniques and stained using a monoclonal antibody to SLPI (Santa Cruz, CA; titer of 1:100) and an avidin-biotin detection kit.

## Results

SLPI expression was observed in all (n=9) cases of the FT epithelium as cytoplasmic staining with no predilection to either ciliated or non-ciliated cells.

SLPI expression was observed in all (n=9) cases of SPC, predominantly in areas retaining a papillary architecture but generally lost in areas of solid tumor growth.

No SLPI expression was noted in any (n=9) cells of the OSE.

	SPC	Normal FT	Normal OSE
Number of cases (n)	9	9	9
SLPI Positive Cases	9	9	0
% of Positive Cases	100%	100%	0

**Table.** Summary of immunohistochemistry results.

## Discussion

The pathogenesis of (ovarian) serous papillary carcinoma, the most lethal gynecologic malignancy, remains unclear. The histogenesis of SPC is among many controversies in this field. Most investigators believe that SPC is derived from the malignant transformation of the single mesothelial surface lining of ovaries or the cells that line superficial cortical inclusion cysts.<sup>2,3</sup> However, it has been noted that the morphology of SPC shares a striking resemblance with that of FT epithelium. Precursor lesions in the fallopian tubes such as atypical epithelial proliferation or carcinoma in situ have been previously documented.<sup>4</sup> These observations raise the possibility that SPC arises from FT epithelium. Marquez *et al.* recently reported that the gene expression pattern of SPC correlates better with that in normal FT (p=0.0042) than in normal OSE (p=0.0743), supporting an FT origin of SPC.<sup>4</sup>

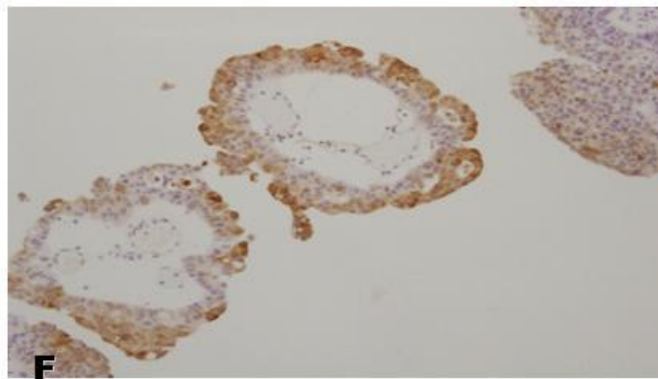
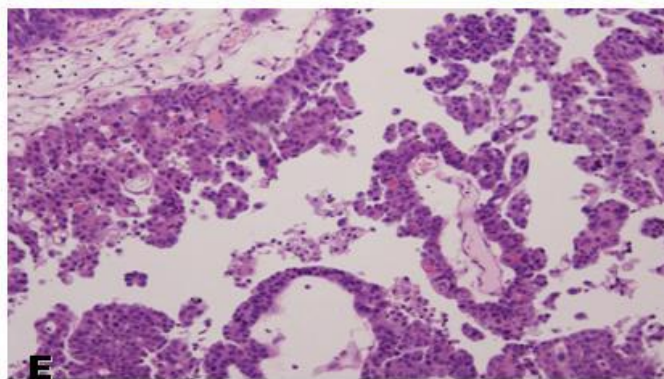
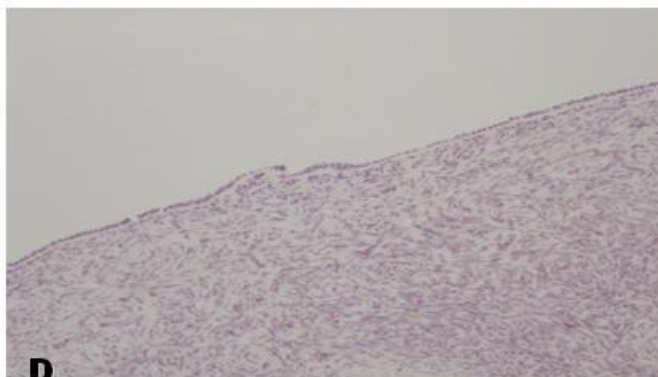
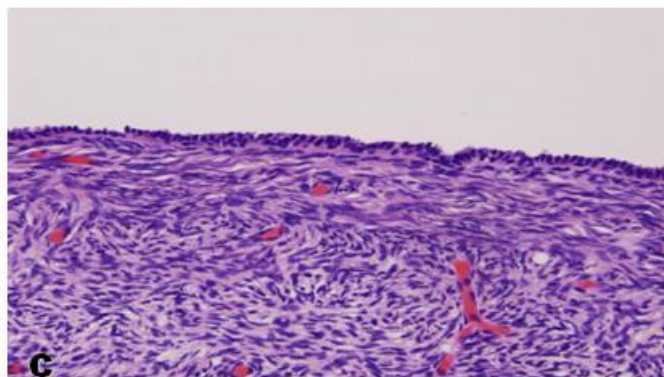
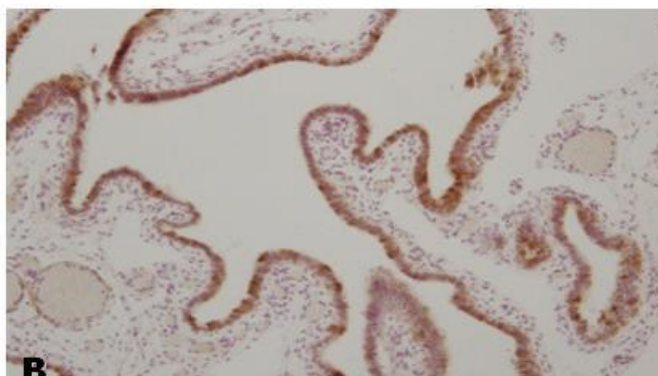
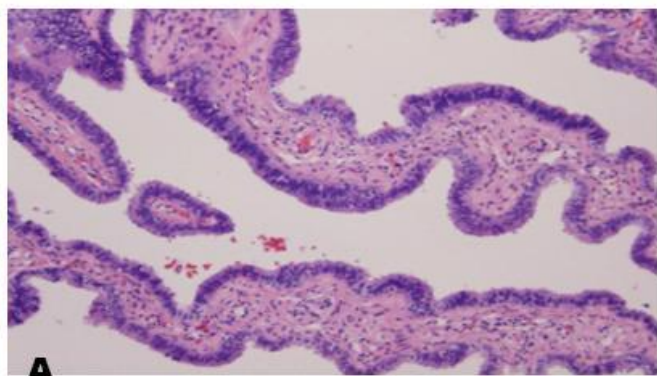
In this study, the expression profile of SLPI in SPC was compared with that in normal FT and normal OSE. Our findings that 100% (9/9) of normal FT and 100% (9/9) of SPC expressed the protein SLPI, whereas none of the normal OSE samples (0/9) expressed the SLPI protein, supports the notion that the cell of origin for SPC may reside in the epithelia of the FT.

### Conclusion

The presence of SLPI in FT epithelium and in SPC but absence in OSE further supports the contention that the FT epithelium may be the cell of origin for SPC.

### References

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H&E (10X)

SLPI (10X)

**Figure.** Panels A & B: Normal Fallopian tube. Panels C & D: Normal ovary. Panels E & F: Serous papillary carcinoma.