

Long-term Adaptive Changes in the Neovaginal Mucosa and Quality of Life Following Sigmoid Colon Vaginoplasty

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Abstract

Objective

Sigmoid colon vaginoplasty is a well-established surgical procedure for vaginal reconstruction. While anatomical success is documented, long-term functional and molecular adaptations of the neovaginal mucosa remain poorly characterized. This study aimed to evaluate the temporal changes in the secretory profile of the sigmoid neovagina and assess the long-term impact on patients' sexual function and quality of life.

Methods

In this cross-sectional study, 38 patients who underwent sigmoid vaginoplasty were stratified into two groups: Short-Term (≤ 4 years post-op, $n = 20$) and Long-Term (≥ 8 years post-op, $n = 18$). Control tissues included normal sigmoid ($n = 15$) and vaginal ($n = 15$) mucosa. Neovaginal biopsies from the apex were analyzed histologically and by immunohistochemistry for secretory markers (MUC2, AQP9, AQP2, CFTR). Participants completed the Female Sexual Function Index (FSFI) and the 36-Item Short Form Health Survey (SF-36).

Results

All patients reported high satisfaction with neovaginal appearance and function. FSFI scores were comparable across all groups, indicating preserved sexual function. SF-36 scores were similar except for the Mental Health domain, which was significantly lower in neovaginal groups. Histologically, long-term neovaginas exhibited glandular atrophy and a significant reduction in goblet cell density. Immunohistochemistry revealed a time-dependent decline in the expression of colonic secretory markers MUC2, AQP9, and CFTR ($p < 0.001$). In contrast, AQP2 expression was significantly elevated in long-term neovaginas and was most abundant in native vaginal tissue.

Conclusion

Sigmoid vaginoplasty provides durable anatomical and functional outcomes. The neovaginal mucosa undergoes a remarkable adaptive process, shifting from a colonic secretory phenotype towards a more vaginal-like phenotype over years. The sustained expression of AQP2 in both native and neovaginal tissues underscores its potential critical role in maintaining mucosal hydration, contributing to satisfactory sexual function despite a reduction in mucus secretion.

1. Introduction

Vaginoplasty is primarily employed for the management of Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, pseudo-hermaphroditism, androgen insensitivity syndrome, vaginal agenesis following pelvic malignancy surgery, and male-to-female gonadal reconstruction. The most prevalent condition is MRKH syndrome, a congenital anomaly resulting from hypoplasia of the Müllerian ducts during embryogenesis, affecting approximately 1 in 4,000 to 5,000 live female births^[1–3]. Clinically, affected individuals exhibit agenesis or underdevelopment of the vagina, uterus, and fallopian tubes, despite possessing normal secondary sexual characteristics and a standard 46,XX karyotype^[2, 3]. Emerging evidence indicates that genetic dysregulation of Wnt and Hox genes, coupled with prenatal environmental stressors, may contribute to female reproductive tract maldevelopment^[4, 5]. The therapeutic aim is to establish a functional neovaginal canal through comprehensive, multidisciplinary approaches, facilitating normal sexual function while addressing the patient's emotional and psychological well-being^[1, 6–8].

The variety of surgical approaches for artificial vaginoplasty, which utilize different graft materials such as amnion, skin flaps, peritoneum, and biological meshes, results in diverse outcomes and inherent limitations^[9–11]. These limitations include stenosis, insufficient length, compromised secretory function, adjacent organ injury, and high costs. The sigmoid colon vaginoplasty, involving the resection of a pedicled segment of the colon, benefits from its rich vascular supply, thicker intestinal wall, favorable elasticity, and robust secretory capacity^[10, 12–15]. Postoperative management typically obviates the need for external dilators, and both morphological and functional parameters closely emulate those of a normal vagina, rendering it one of the most prevalent clinical techniques^[10, 12–15]. However, this procedure entails considerable trauma and elevated risk, with postoperative secretion of copious, malodorous mucus, which can be distressing to patients^[10, 12, 14]. Current literature predominantly focuses on short-term surgical outcomes and anatomical success, with a notable knowledge gap regarding the long-term biological fate of the transplanted intestinal segment within the unique pelvic environment^[10, 16–18]. Given that the colon's mucosa, originally adapted for fecal passage, is suddenly exposed to a novel biomechanical and microbiological milieu, understanding its molecular-level adaptation remains a fundamental issue in reconstructive gynecology^[16–18].

In the colon, mucin 2 (MUC2) serves as the core gel-forming component of the mucosal barrier matrix. Its proper polymerization and secretion are critical for isolating intestinal microbiota and maintaining internal homeostasis^[19, 20]. Aquaporins (AQPs) are a family of membrane proteins that facilitate water transport across biological membranes, playing an essential role in cellular and tissue water regulation^[21]. AQP-9, a broadly expressed permeability-selective channel predominantly found in hepatocytes and leukocytes, is associated with inflammatory and infectious responses. Multiple studies have demonstrated that AQP-9 is expressed in the colon and may be involved in colonic secretion processes^[21]. Aquaporin-2 (AQP-2), a key arginine vasopressin-regulated water channel, is localized primarily in the principal cells of renal collecting ducts, where it plays a pivotal role in urine concentration and systemic water homeostasis^[22]. Recent reproductive-tract aquaporin reviews indicate that AQP-mediated water transport contributes to female reproductive tract fluid balance, including vaginal and

cervical lubrication, supporting the rationale for evaluating AQP-2 in neovaginal hydration^[23]. Within the digestive system, the cystic fibrosis transmembrane conductance regulator (CFTR) facilitates chloride ion and bicarbonate secretion, playing an indispensable role in ionic balance and acid-base homeostasis^[24]. This study longitudinally follows patients who have undergone sigmoid colon vaginoplasty, focusing on postoperative quality of life and changes in artificial vaginal secretion function—specifically assessing MUC-2, AQP-9, AQP-2, and CFTR expression—to scientifically evaluate the morphological and functional adaptive changes of the neovagina.

2. Materials and Methods

2.1. Study Population and Ethical Approval

This study conducted a follow-up on 208 patients who underwent sigmoid colon–vaginal substitution vaginoplasty at our institution from January 1999 to November 2011, with 43 patients returning for follow-up, resulting in a follow-up rate of 20.7%. The research was approved by the institutional ethics committee, and all participants provided informed consent. Ultimately, 38 patients were included and divided into two groups based on postoperative duration: a short-term group (≤ 4 years, $n = 20$) and a long-term group (≥ 8 years, $n = 18$). The control tissues were obtained from: (a) the normal sigmoid colon mucosa of patients undergoing sigmoid colon–vaginal substitution at the same time (normal sigmoid colon group, $n = 15$), and (b) the normal vaginal mucosa of women undergoing surgery for other diseases at the same time (normal vaginal mucosa group, $n = 15$). Patients with gastrointestinal diseases, a history of hormone or immunosuppressive therapy, or with local or systemic acute inflammation were excluded from the study.

2.2. Data and Specimen Collection

All participants underwent standardized interviews and gynecological examinations, and completed the FSFI^[25] and SF-36^[26] questionnaires. In the study group, mucosal biopsy specimens were collected from the upper third of the vagina via artificial vaginal sampling. (Short-term group: 15 cases; long-term group: 13 cases.)

2.3. Histology and Immunohistochemistry

Organized tissue samples were fixed in 4% paraformaldehyde, embedded in paraffin, and sectioned. Hematoxylin and eosin (H&E) staining was performed for morphological evaluation.

Immunohistochemistry was conducted using the SP method; following antigen retrieval and serum blocking, sections were incubated overnight at 4°C with primary antibodies against MUC2, AQP2, AQP9, and CFTR. Subsequently, DAB was used for chromogenic development. Replacing the primary antibody with PBS served as a negative control, which yielded negative results in all cases.

2.4. Image Analysis

For each case, six high-power fields (400x) were randomly selected from six different sections for imaging. The integrated optical density (IOD) of the positive immunostaining was quantified using Image-Pro Plus 6.0 software.

2.5. Statistical Analysis

Statistical analysis was performed using SPSS 13.0. Continuous data were expressed as mean $\pm$ standard deviation. Intergroup comparisons were conducted using one-way ANOVA or the Kruskal-Wallis test. A p-value of less than 0.05 was considered indicative of statistically significant differences.

3. Results

3.1. Patient Characteristics and Anatomical Outcomes

Postoperative follow-up duration ranged from 10 to 163 months. All patients (100%) expressed satisfaction with the appearance of the neovagina. The average depth of the neovagina was 8-12 cm, with a width of 3-4 cm. The mucosa was pliable, moist, and elastic. Excessive mucous secretion typically diminished within approximately 6.71 ± 2.13 months after surgery.

3.2. Sexual Function and Quality of Life

There were no significant differences in the total FSFI scores or in any of its domains (desire, excitement, lubrication, orgasm, satisfaction, pain) among the short-term, long-term, and normal vaginal groups (Table 1), indicating preserved sexual function. In the SF-36 assessment, scores across dimensions such as physical functioning, role limitations due to physical health, bodily pain, general health, vitality, social functioning, and role limitations due to emotional problems showed no significant differences among the groups. However, the mental health scores in both the neovaginal groups were significantly lower than those of the normal vaginal group ($p=0.001$) (Table 2).

3.3. Histological Changes

H&E staining reveals that the normal sigmoid colon mucosal glands are densely packed, uniformly distributed, and rich in goblet cells. The short-term neovaginal group exhibits glands of variable size. In stark contrast, the long-term neovaginal group shows a significant reduction in both gland number and volume, with a marked decrease in the percentage of goblet cells within each gland (from over 80% to less than 40%). Some glands even lack goblet cells entirely (Figure 1).

3.4. Molecular Marker Expression

MUC2: MUC2 is primarily expressed in goblet cell mucins. In normal sigmoid colon goblet cells, MUC2 expression is abundant, but shows a progressive and significant decrease in the neovagina group, reaching the lowest levels in the long-term neovagina group ($p<0.001$). No MUC2 expression is observed in normal vaginal tissue (Figure 2, Table 3).

AQP-9: AQP-9 is mainly expressed in the cytoplasm of glandular cells. Strong expression of AQP-9 is observed in normal sigmoid colon and short-term neovagina, but significantly decreases in the long-term neovagina group ($p < 0.001$). Normal vaginal tissue is negative for AQP-9 expression (Figure 3, Table 3).

AQP-2: AQP-2 is primarily expressed in the cytoplasm of glandular cells. In normal sigmoid colon, AQP-2 expression is weak; however, it shows a significant increase in the long-term neovagina group ($p < 0.01$). Notably, AQP-2 exhibits the strongest expression in the basal and parabasal layers of normal vaginal stratified squamous epithelium ($p < 0.001$ compared to all other groups) (Figure 4, Table 4).

CFTR: CFTR is mainly expressed in the cytoplasm of glandular cells, with occasional nuclear expression. In normal sigmoid colon, CFTR shows high expression levels, which remain stable in the short-term group but decline significantly in the long-term group ($p < 0.001$). In normal vaginal tissue, weak but distinct CFTR expression is observed, with levels significantly lower than those in normal sigmoid colon and short-term groups (Figure 5, Table 4).

4. Discussion

The primary goal of vaginoplasty is to construct a neovagina in patients with congenital vaginal agenesis or severe vaginal dysgenesis that mimics the anatomical and functional characteristics of a natural vagina, thereby restoring sexual function and psychological well-being^[1, 3, 6-8]. Over more than a century of development, surgical techniques have continually evolved—from early methods such as the compression technique and skin flap transplantation to the utilization of peritoneal, amniotic membrane, and various intestinal segments—reflecting an ongoing clinical pursuit for more optimal reconstructive outcomes^[9-11]. Among these, sigmoid colon vaginoplasty has consistently maintained a significant role since its initial application^[10, 12-15]. A comprehensive comparison of different techniques reveals that its advantages are notably prominent:

1. **Anatomical Benefits:** The luminal diameter of the sigmoid colon closely resembles that of the natural vagina, with a long mesentery and reliable blood supply, enabling one-stage creation of a sufficiently deep (typically >10 cm) and wide vaginal canal. It also resists contraction, thus avoiding the necessity of long-term mold wearing and the risk of stenosis associated with peritoneal or skin flap methods^[10, 12-15].

2. **Functional Benefits:** The mucosa of the sigmoid segment is inherently moist and soft, possessing natural secretory functions that provide essential lubrication for sexual activity—a feature difficult to replicate with non-mucosal grafts^[10, 12-15].

However, this approach also presents unavoidable drawbacks, such as relatively extensive surgical trauma, potential abdominal complications, and early postoperative issues like excessive mucus secretion and malodor^[10, 12, 14, 15]. Therefore, in-depth investigation of its long-term outcomes, especially the fate of the transplanted intestinal segment within the new environment, holds significant clinical

importance^[16-18]. This study, through long-term follow-up, evaluates the adaptive changes of the sigmoid colon neovagina from patient-reported outcomes, tissue morphology, and molecular functional perspectives, providing new evidence to deepen our understanding of the benefits and limitations associated with this technique.

Firstly, regarding the aspects of sexual activity and quality of life that patients prioritize most, this study confirms the long-term efficacy of sigmoid colon vaginoplasty while also highlighting the need for ongoing attention to psychosocial aspects. Our data demonstrate that postoperative patients, whether in the short- or long-term follow-up, have FSFI scores across various domains comparable to those of healthy controls, consistent with most reports both domestically and internationally^[6, 10, 12-15]. This underscores the functional reliability of the sigmoid colon neovagina in providing satisfactory sexual experiences: its adequate depth and diameter prevent dyspareunia, while the persistent mucosal lubrication effectively addresses the core issue of lubrication deficiency. However, the SF-36 results reveal a noteworthy phenomenon: despite excellent scores in physical and social functioning, patients' "mental health" dimension scores are significantly lower than those of normal controls. This suggests that successful surgical reconstruction does not automatically equate to complete psychological healing. Patients, diagnosed during puberty and undergoing surgery before integrating into intimate relationships, often experience intense stigma, anxiety, and body image concerns throughout the process. Even with good sexual function recovery, these profound psychological effects may persist in the long term^[7, 8]. Therefore, for patients undergoing vaginoplasty, specialized psychological support and counseling during the perioperative period and long-term follow-up should be regarded as equally essential components of comprehensive medical care alongside the surgical intervention^[1, 7, 8].

Secondly, and most critically, our study reveals that the transplanted sigmoid colon mucosa undergoes significant and orderly adaptive changes within the vaginal environment, with its "secretory function" continuously evolving. Traditional perspectives often regard the postoperative reduction in mucus secretion as a positive development, a mitigation of complications. However, our histological and molecular biological findings depict a more complex scenario: over time (notably in the long-term group of ≥ 8 years), the neovaginal mucosa exhibits progressive simplification of glandular structures and a reduction in goblet cell density. This finding is consistent with recent work emphasizing that neovaginal epithelial and microbiological characteristics are shaped by tissue origin, local niche conditions, and postoperative remodeling^[16-18]. Correspondingly, the expression levels of key secretory molecules such as MUC2, involved in mucin production; AQP9, associated with glycerol and water transport; and CFTR, a critical chloride channel driving fluid secretion, all demonstrate a significant, time-dependent decline^[19-21, 24]. These molecular insights directly clarify the clinical observation of decreasing postoperative mucus production, representing an adaptive "de-functionalization" remodeling of colonic mucosa in response to the "non-fecal passage" environment.

However, a more insightful discovery pertains to the changes in the expression of aquaporin 2 (AQP2). Contrary to the trends observed with the aforementioned proteins, AQP2 expression is markedly

increased in the long-term neovaginal mucosa compared to normal colon and short-term groups. Notably, the strongest AQP2 immunoreactivity was detected in the basal and parabasal layers of normal vaginal stratified squamous epithelium. AQP2 is classically regulated by vasopressin and is predominantly expressed in the principal cells of renal collecting ducts, where it mediates water reabsorption^[22]. Recent studies have increasingly identified aquaporin-mediated water transport in various peripheral tissues, including the female reproductive tract, suggesting a role in local fluid balance regulation and mucosal lubrication^[23]. We hypothesize that in the sigmoid colon-derived neovagina, as the colonic active secretion mechanism—centered around MUC2, AQP9, and CFTR—diminishes, the mucosa may adapt by upregulating AQP2 expression to enhance the absorption and trans-epithelial transport of interstitial fluid or vascular exudate^[19-24]. This adaptation could shift towards a “moist” maintenance mode characterized by passive exudation and reabsorption, more closely resembling the vaginal environment. This phenotypic transition from “active secretion” to “passive humidification” represents a profound, functional tissue adaptation aimed at reducing excess mucus secretion while preserving a necessary level of moisture.

In summary, sigmoid colon vaginoplasty is not a static “transplantation” procedure but initiates a dynamic biological process of “integration and adaptation.” Our study confirms its long-term anatomical stability and functional outcomes, highlighting the necessity of enhancing psychological interventions within the mind-body paradigm^[7, 8, 10, 12-15]. More importantly, we reveal at the molecular level that the new vaginal mucosa undergoes intrinsic functional remodeling to adapt to its new environment, with a significant shift in secretory phenotype from colonic to vaginal characteristics^[16-24]. This discovery not only deepens our understanding of the physiological basis of this surgical approach but also provides a theoretical foundation for further optimization of surgical techniques, such as exploring ideal bowel segment lengths and handling methods. Investigating how local pharmacological or biological modulation can more precisely guide this adaptive process to balance excessive secretion and adequate moisture retention presents a promising area for future research.

Declarations

Authors’ contributions Conceptualization, X.H.H., and; methodology, Y.F.D.; formal analysis, L.L.C., P.L., M.L.Z., and L.Z.; data curation, Y.L.X., J.H.Z., H.J.S., and X.H.H.; writing—original draft preparation, L.L.C.; writing—review and editing, J.H.Z. All authors have read and agreed to the published version of the manuscript.

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Data availability The datasets used and/or analyzed during the current study are available from the corresponding authors on reasonable request.

Ethics approval and consent to participate This study followed the guidelines of the Declaration of Helsinki and was approved by the Ethics Review Board of the Second Hospital of Hebei Medical

University. All participants provided informed consent prior to their inclusion in the study.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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Tables

Table 1. Female Sexual Function Index (FSFI) scores by group

Variable	Short-term group (n=20)	Long-term group (n=18)	Normal vaginal controls (n=30)	P value
Sexually active participants, n	20	18	30	
Total FSFI score	25.30 ± 3.58	25.37 ± 3.62	26.54 ± 3.52	0.467
FSFI score category, n				0.617
≥30	4	4	7	
24–29	10	9	16	
≤23	6	5	7	
Sexual desire	3.42 ± 0.96	3.50 ± 1.05	3.74 ± 1.08	0.526
Sexual arousal	3.87 ± 0.80	3.98 ± 0.86	4.11 ± 0.93	0.634
Vaginal lubrication	4.95 ± 0.72	4.88 ± 0.67	4.85 ± 0.64	0.875
Orgasm	3.92 ± 0.94	3.87 ± 0.93	4.24 ± 0.86	0.295
Sexual satisfaction	4.36 ± 0.83	4.28 ± 0.77	4.57 ± 0.75	0.419
Pain	4.78 ± 0.62	4.86 ± 0.59	5.03 ± 0.64	0.370

Values are presented as mean ± SD unless otherwise indicated. The normal vaginal controls in Tables 1 and 2 are questionnaire controls (n=30), distinct from the normal vaginal tissue controls used for histology and immunohistochemistry (n=15). The P value for FSFI score category distribution was calculated using the χ^2 test.

Table 2. 36-Item Short Form Health Survey (SF-36) scores by group

Domain	Short-term group (n=20)	Long-term group (n=18)	Normal vaginal controls (n=30)	P value
Physical functioning (PF)	94.0 ± 6.20	93.1 ± 10.5	95.5 ± 4.2	0.780
Role-physical (RP)	90.0 ± 12.6	88.9 ± 15.4	91.7 ± 13.7	0.751
Bodily pain (BP)	89.4 ± 7.8	88.3 ± 13.6	91.6 ± 7.6	0.577
General health (GH)	70.5 ± 8.7	69.7 ± 12.7	71.5 ± 7.7	0.816
Vitality (VT)	78.5 ± 9.6	77.8 ± 13.5	80.0 ± 7.3	0.882
Social functioning (SF)	93.1 ± 10.3	92.4 ± 10.6	95.4 ± 7.0	0.637
Role-emotional (RE)	88.4 ± 19.5	87.1 ± 20.0	92.2 ± 16.7	0.556
Mental health (MH)	69.6 ± 10.5	67.7 ± 14.0	79.1 ± 7.6	0.001

Values are presented as mean ± SD. For the Mental Health domain, the normal vaginal questionnaire control group scored higher than both neovaginal groups in pairwise comparisons (P=0.001 for each comparison).

Table 3. Immunohistochemical expression of MUC2 and AQP9 in epithelial tissues

Marker	Normal sigmoid colon (n=15)	Short-term neovagina (n=15)	Long-term neovagina (n=13)	Normal vaginal tissue (n=15)	P value
MUC2	3294.8 ± 291.0	2462.6 ± 217.0	1148.5 ± 193.4	Not detected	<0.001
AQP9	430.8 ± 91.6	390.6 ± 77.4	190.5 ± 58.0	Not detected	<0.001

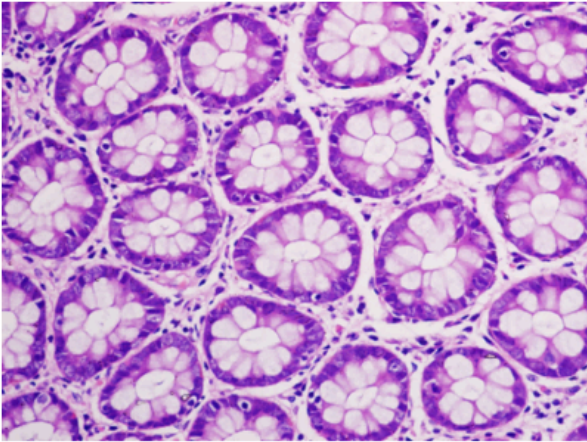
Values are integrated optical density (IOD), presented as mean ± SD. The P values refer to overall comparisons among the three quantified tissue groups: normal sigmoid colon, short-term neovagina, and long-term neovagina. MUC2: all pairwise comparisons among the three quantified tissue groups were significant (P<0.05). AQP9: the long-term neovagina group differed significantly from both the normal sigmoid colon and short-term neovagina groups (P<0.05), whereas the normal sigmoid colon and short-term neovagina groups did not differ significantly.

Table 4. Immunohistochemical expression of AQP2 and CFTR in epithelial tissues

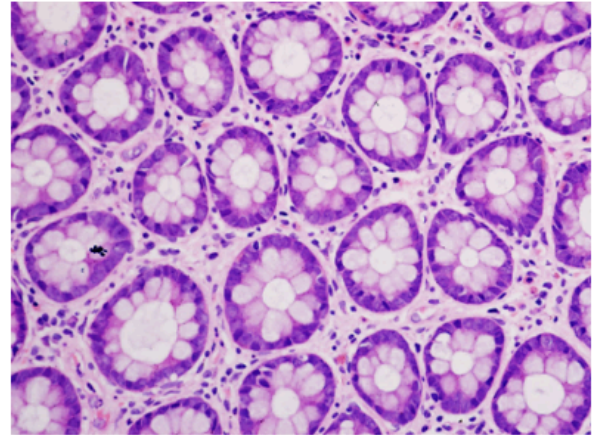
Marker	Normal sigmoid colon (n=15)	Short-term neovagina (n=15)	Long-term neovagina (n=13)	Normal vaginal tissue (n=15)	P value
AQP2	260.6 ± 61.7	278.6 ± 67.9	359.3 ± 89.6	548.0 ± 76.2	<0.001
CFTR	763.9 ± 92.4	747.3 ± 52.4	402.9 ± 57.2	374.0 ± 57.4	<0.001

Values are integrated optical density (IOD), presented as mean $\pm$ SD. AQP2: the long-term neovagina group was higher than the normal sigmoid colon and short-term neovagina groups ($P<0.05$), and the normal vaginal tissue group was higher than all other groups ($P<0.05$). CFTR: the long-term neovagina group was lower than the normal sigmoid colon and short-term neovagina groups ($P<0.05$); the normal vaginal tissue group was lower than the normal sigmoid colon and short-term neovagina groups ($P<0.05$) but did not differ significantly from the long-term neovagina group ($P=0.261$).

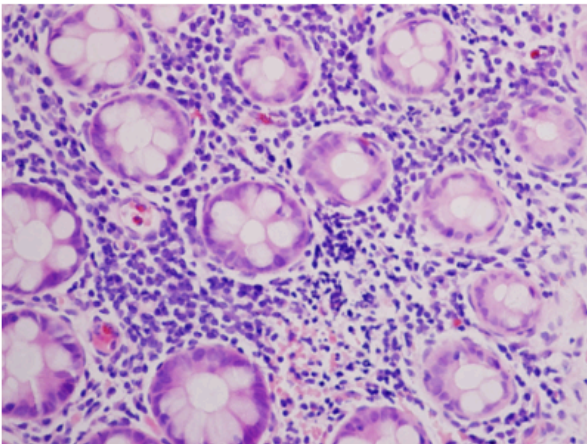
Figures



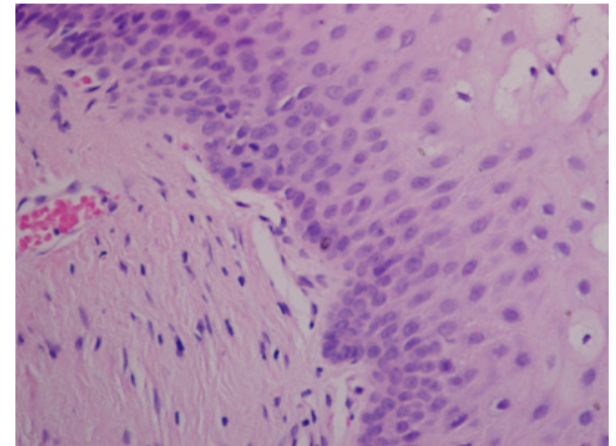
A1



A2



A3



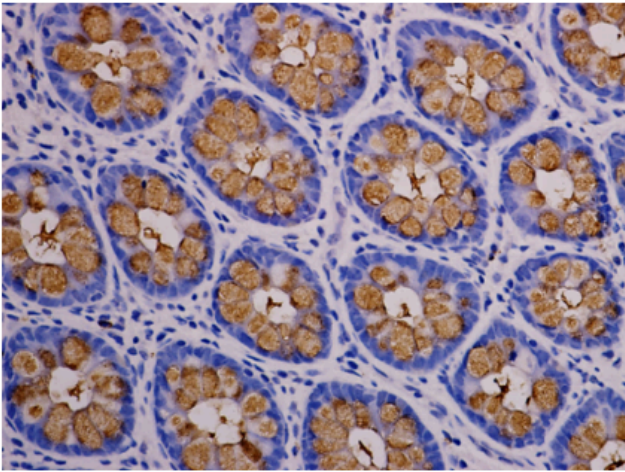
A4

Figure 1

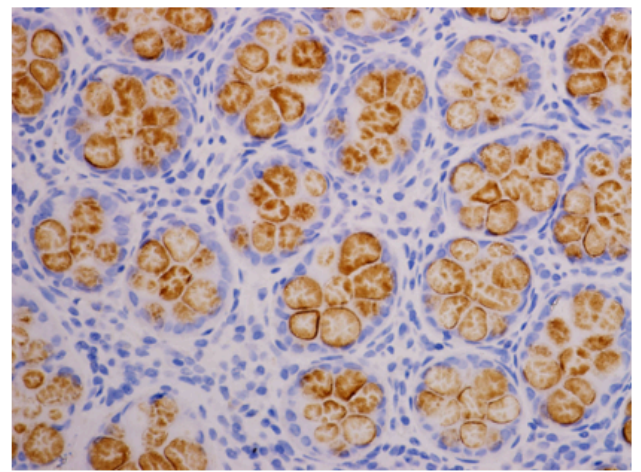
Representative histological features of sigmoid neovaginal mucosa and control tissues.

Hematoxylin and eosin (H&E) staining; original magnification $\times 400$. (A1) Normal sigmoid colon mucosa. (A2) Sigmoid neovaginal mucosa approximately 3 years after surgery. (A3) Sigmoid neovaginal mucosa

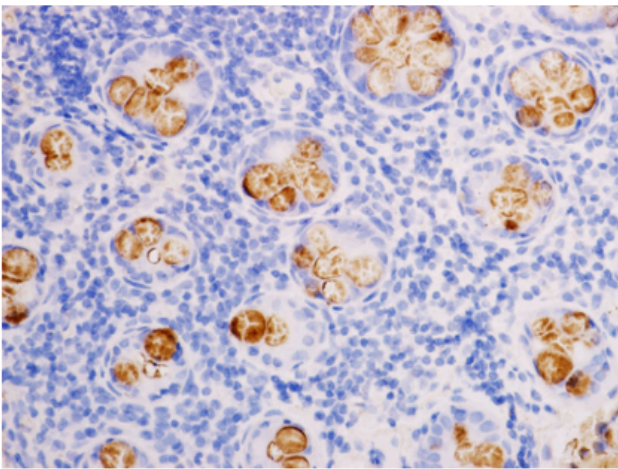
approximately 10 years after surgery, showing reduced gland density and fewer goblet cells. (A4) Normal vaginal mucosa.



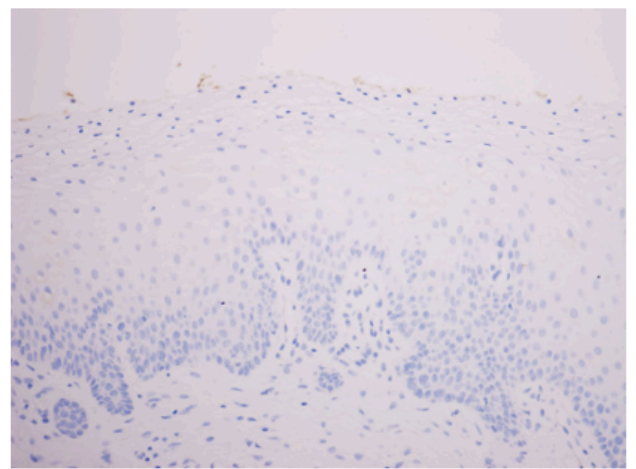
B1



B2



B3

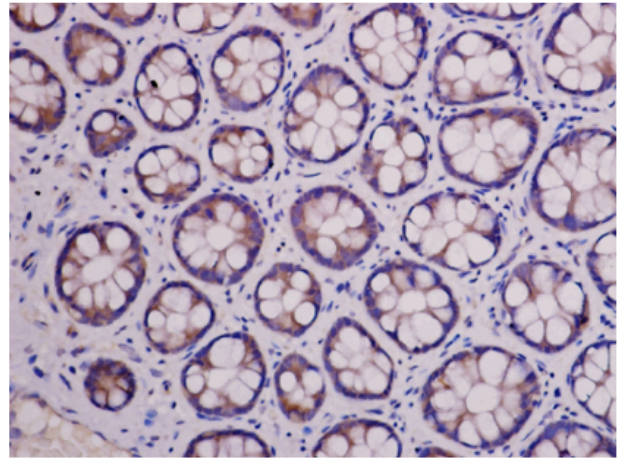
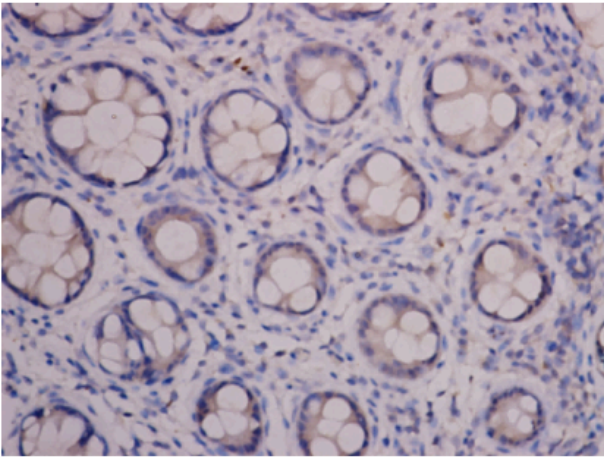


B4

Figure 2

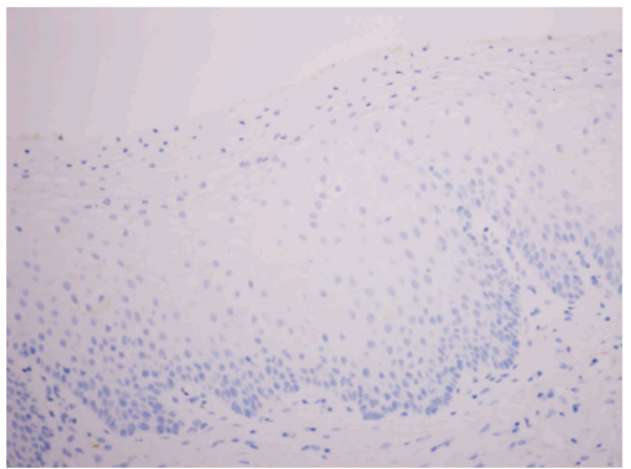
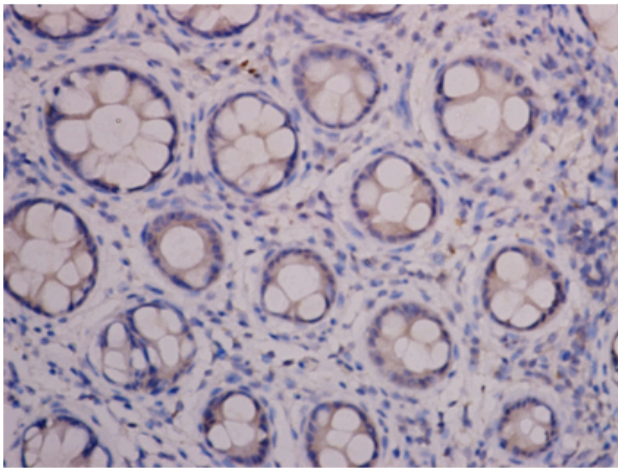
Representative immunohistochemical staining for mucin 2 (MUC2)

original magnification $\times 400$. (B1) Normal sigmoid colon mucosa. (B2) Sigmoid neovaginal mucosa approximately 3 years after surgery. (B3) Sigmoid neovaginal mucosa approximately 10 years after surgery. (B4) Normal vaginal mucosa. MUC2 immunoreactivity is strongest in normal sigmoid colon, decreases in the long-term neovaginal mucosa, and is not detected in normal vaginal mucosa.



C1

C2



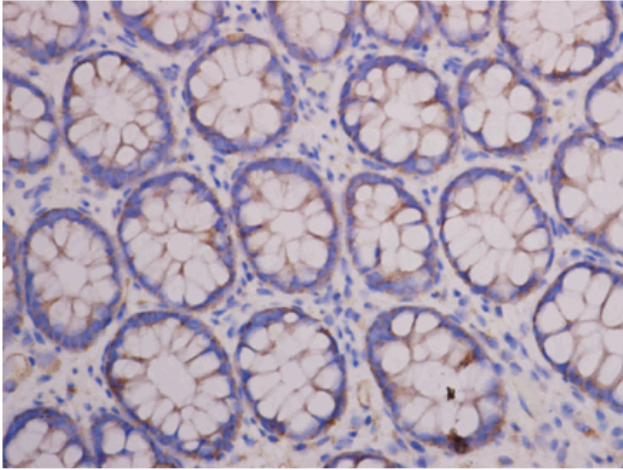
C3

C4

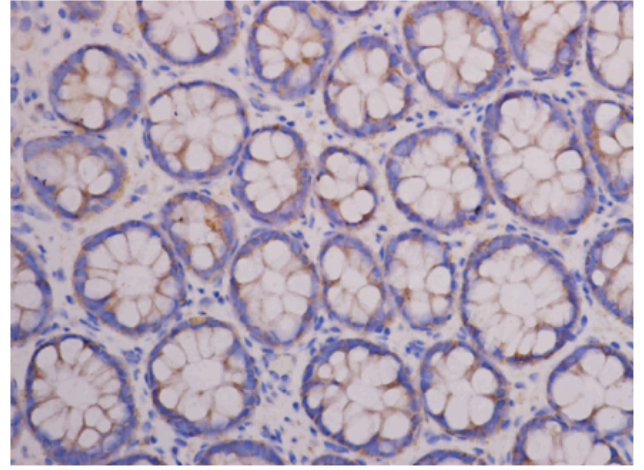
Figure 3

Representative immunohistochemical staining for aquaporin 9 (AQP9)

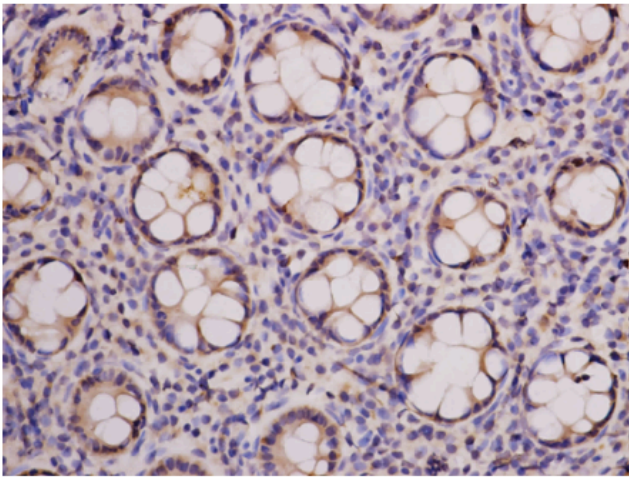
original magnification $\times 400$. (C1) Normal sigmoid colon mucosa. (C2) Sigmoid neovaginal mucosa approximately 3 years after surgery. (C3) Sigmoid neovaginal mucosa approximately 10 years after surgery. (C4) Normal vaginal mucosa. AQP9 immunoreactivity is retained in short-term neovaginal mucosa but reduced in long-term neovaginal mucosa; normal vaginal mucosa is negative.



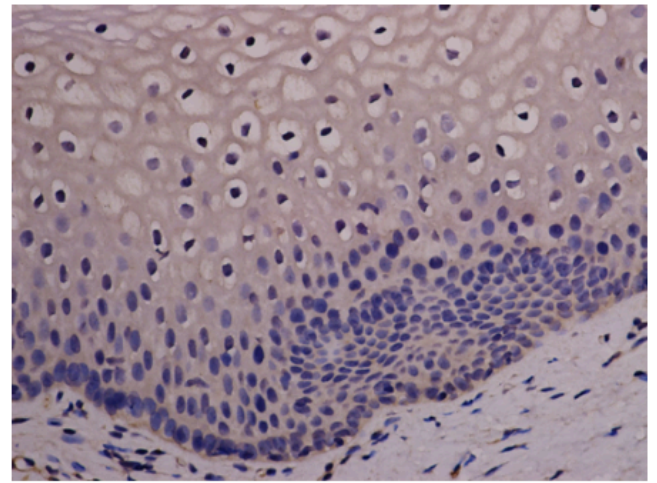
D1



D2



D3

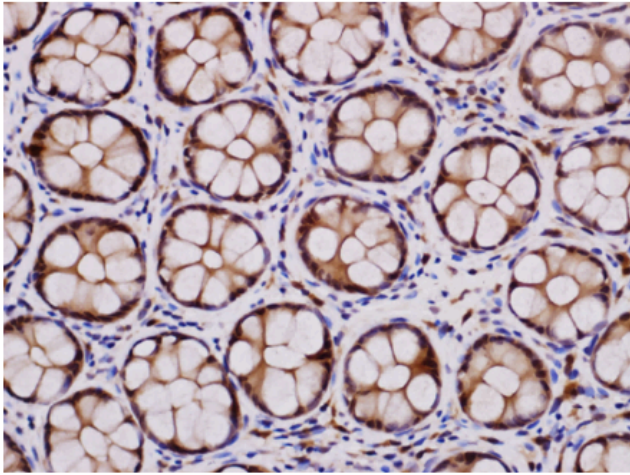


D4

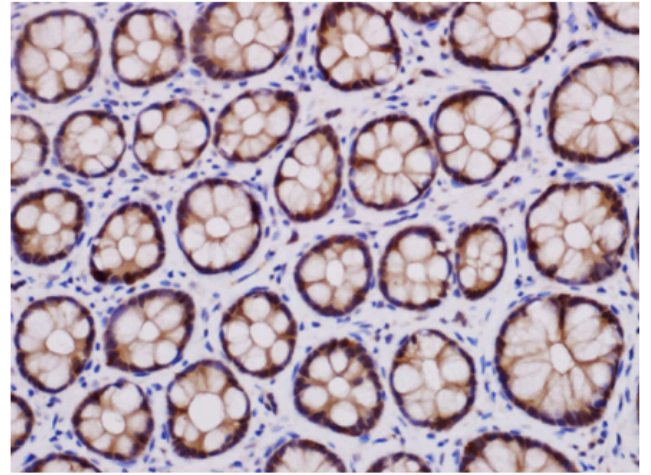
Figure 4

Representative immunohistochemical staining for aquaporin 2 (AQP2)

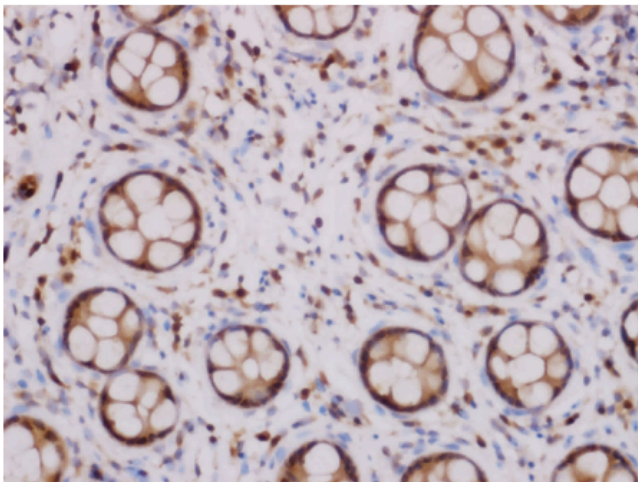
original magnification $\times 400$. (D1) Normal sigmoid colon mucosa. (D2) Sigmoid neovaginal mucosa approximately 3 years after surgery. (D3) Sigmoid neovaginal mucosa approximately 10 years after surgery. (D4) Normal vaginal mucosa. AQP2 expression is weak in normal sigmoid colon and short-term neovaginal mucosa, increases in long-term neovaginal mucosa, and is strongest in the basal and parabasal layers of normal vaginal epithelium.



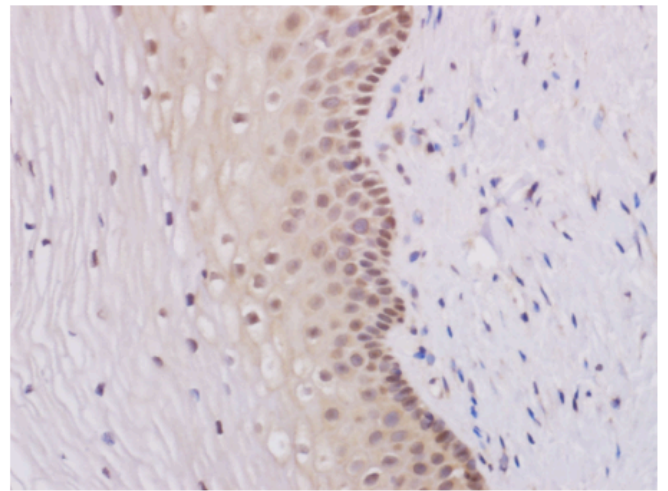
E1



E2



E3



E4

Figure 5

Representative immunohistochemical staining for cystic fibrosis transmembrane conductance regulator (CFTR)

original magnification $\times 400$. (E1) Normal sigmoid colon mucosa. (E2) Sigmoid neovaginal mucosa approximately 3 years after surgery. (E3) Sigmoid neovaginal mucosa approximately 10 years after surgery. (E4) Normal vaginal mucosa. CFTR expression is high in normal sigmoid colon and short-term neovaginal mucosa, decreases in long-term neovaginal mucosa, and is weakly present in normal vaginal epithelium.