Data in Brief 48 (2023) 109243

Contents lists available at ScienceDirect

Data in Brief

journal homepage: www.elsevier.com/locate/dib

Data Article

Dataset on mucin 1 and 4 proteins and SialyT and T antigens staining patterns in cervical cancer primary tumors and metastatic lymph nodes

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ARTICLE INFO

Article history:
Received 2 May 2023
Revised 9 May 2023
Accepted 11 May 2023
Available online 18 May 2023

Dataset link: MUC1, MUC4, Stn, TN dataset in cervical cancer (Original data)

Keywords:
Cervical cancer
Lymph node
Metastasis
Photomicrograph
Sialyl T antigen
MUC
Glycoprotein
Biomarker

ABSTRACT

The objective was to find an association between abnormal glycosylation, represented by Tn and STn antigens on mucin (MUC) proteins, in primary tumor specimens with lymph node metastasis or recurrence of cervical cancer patients. Prospectively collected specimens were obtained from the NRG Oncology/GOG clinical trial GOG 0221 patients with previously untreated stage IB-IVA primary cervical cancer, who underwent surgical resection and removal of associated para-aortic and pelvic lymph nodes. Immunohistochemical staining for mucin 1 and 4 (MUC1 and MUC4) proteins and surface glycoproteins Tn and Sialyl Tn were performed on sections cut from formalin-fixed, paraffin-embedded specimen blocks. Loss vs no loss, of immunohistochemical stain upon neuraminidase treatment was used to verify STn vs Tn positivity, respectively, in patient specimens and in colon tissue from wild-type and T-synthase knockout transgenic mice, which served as STn positive versus STn negative controls, respectively. H-scores of staining intensity and percentage of cells stained was performed by experienced gynecologic pathologists. An experienced gynecologic pathologist also

DOI of original article: 10.1016/j.ygyno.2023.02.001
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https://doi.org/10.1016/j.dib.2023.109243

selected photographed regions of interest associated with these cases. The photomicrographs presented in this data set highlight the spectrum of morphologic expression and variability in glycoprotein expression in primary tumors and cancer-positive lymph node specimens. Findings may prove useful in furthering the understanding of cervical cancer glycoproteins, creation of artificial intelligence immunohistochemical scoring systems, and the development of targeted drug therapy.

Specifications Table

Subject	Health and Medical Science - Gynecology
Specific subject area	Biomarkers analysis that identify lymph node metastases in cervical cancer
Type of data	Immunohistochemistry images and Tables
How the data were acquired	Nikon Eclipse Ni microscope (Minato City, Tokyo, Japan) utilizing NIS-Elements AR 3.2 64-bit software. Evaluation of IHC slides and photography with annotation by experienced gynecologic pathologists, blinded to clinical parameters. Stain intensity was graded (0 = no stain, 1 = weak, 2 = moderate, 3 = strong) along with the percentage of positive cells (0–100%).
Data format	Digital photomicrographs (Raw images) organized into figures (TIF). *Analyzed histological scores (xlsx, raw data attached with this article.*
Description of data collection	The photomicrographs are images of immunohistochemically stained cervical cancer and lymph node metastases. The specimens were prospectively collected from patients enrolled in the Gynecologic Oncology Group (GOG) clinical trial GOG0221: Glycoprotein and glycan profiling in patients with locally advanced cervical cancer (Stage IB2, IIA > 4 cm, IIB to IVA) undergoing pelvic and para-aortic (abdominal) lymphadenectomy (clinicaltrials.gov:NCT00460356). Sections of the specimens immunohistochemically stained for mucin 1 and 4 proteins (MUC1 and MUC4, respectively) and Sialyl Tn (STn) and Tn antigens were reviewed by experienced gynecologic pathologists and areas of interest for photomicrography were selected by the first two authors of this brief (R.R. and R.C.). Representative images for all immunohistochemical stains showing their expression patterns as well as positive and negative controls were shown and described. Immunohistochemical staining scores of all antibodies for all specimens are organized into Excel files.
Data source location	• *Institution:* Gynecologic Oncology Section, Obstetrics and Gynecology Department, Stephenson Cancer Center, University of Oklahoma Health Sciences Center • *City/Town/Region:* Oklahoma City, OK • *Country:* USA • *Latitude and longitude (and GPS coordinates, if possible) for collected samples/data:* 35.451918, −97.508469 • (35° 28′54.9048″ N; 97° 30′ 30.4884″ W)
Data accessibility	*Raw data is with the article. Images are available via Mendeley Data.* Repository name: Mendeley Data and Digital Commons Data identification number: 10.17632/h2th44bw8z.1 Direct URL to data: https://data.mendeley.com/datasets/h2th44bw8z/1
Related research article	Benbrook DM, Deng W, Gold MA, Rai R, Conrad R, van der Wel H, Husain S, Moore K, Spirtos N, Jackson AL, Zakhour M, Mathews CA, West CM. Association of Sialyl Tn antigen with cervical cancer lymph node status: An NRG oncology/GOG study. Gynecol Oncol. 2023 Apr;171:67–75. doi: 10.1016/j.ygyno.2023.02.001 [1].

Value of the Data

- This data set highlights the spectrum of morphologic expression and variability in glycoprotein expression for Sialyl Tn, Tn, MUC1, and MUC4 in cervical cancer primary tumors and lymph node metastases. H-scores of the staining reported in the companion article published in the journal *Gynecologic Oncology* document that low STn staining in the primary lesion is associated with reduced lymph node metastases. Photomicrographs communicate a large amount of highly pertinent tumor data (tumor histology, intracellular localization, intratumoral localization, percentage of cells staining, strength of staining, etc.) in a very concise visual fashion.
- These data will be helpful for researchers studying the involvement of glycoproteins in metastasis, particularly for those developing biomarkers and targeted drugs for cervical cancer.
- The finding that low STn expression in the primary tumor is associated with reduced metastases identifies STn as a candidate biomarker and mediator of metastases. This finding warrants further studies to validate reduced primary tumor STn expression as a biomarker of metastases and evaluation of how it contributes to the metastatic process. Further studies could target STn in imaging modalities and strategies to prevent metastases and potentially cervical cancer recurrence. While the overall staining score reported in the companion article reports evaluation of the H-score only, the patterns of glycoprotein expression in primary tumors and metastatic lesions could also be meaningful in research endeavoring to detect and prevent metastasis. Artificial intelligence (AI) computerized immunohistochemical scoring systems could be developed to quantify these patterns for further analysis of their predictive value, which would warrant their development as biomarkers of metastases and their use in studies endeavoring to produce metastases prevention strategies.

1. Objective

This dataset was generated to add value to the original manuscript “Association of Sialyl Tn antigen with cervical cancer lymph node status: An NRG oncology/GOG stud” by providing detailed histologic images and qualitative interpretation beyond the statistical approach used in the primary study.

2. Data Description

The data consist of photomicrographs of all immunohistochemical stains of four representative cases. Figs. 1 and 2 show matching primary tumor and lymph node metastasis specimens from two individual patients, Fig. 3 shows a primary tumor and Fig. 4 shows a lymph node metastasis. These specimens were chosen based on their representation of the range of staining patterns observed in this study. The positive and negative controls for the STn and Tn staining are provided in Fig. 3 of the companion *Gynecologic Oncology* article, and for the MUC1 and MUC4 staining in Fig. 5 of this Data in Brief.

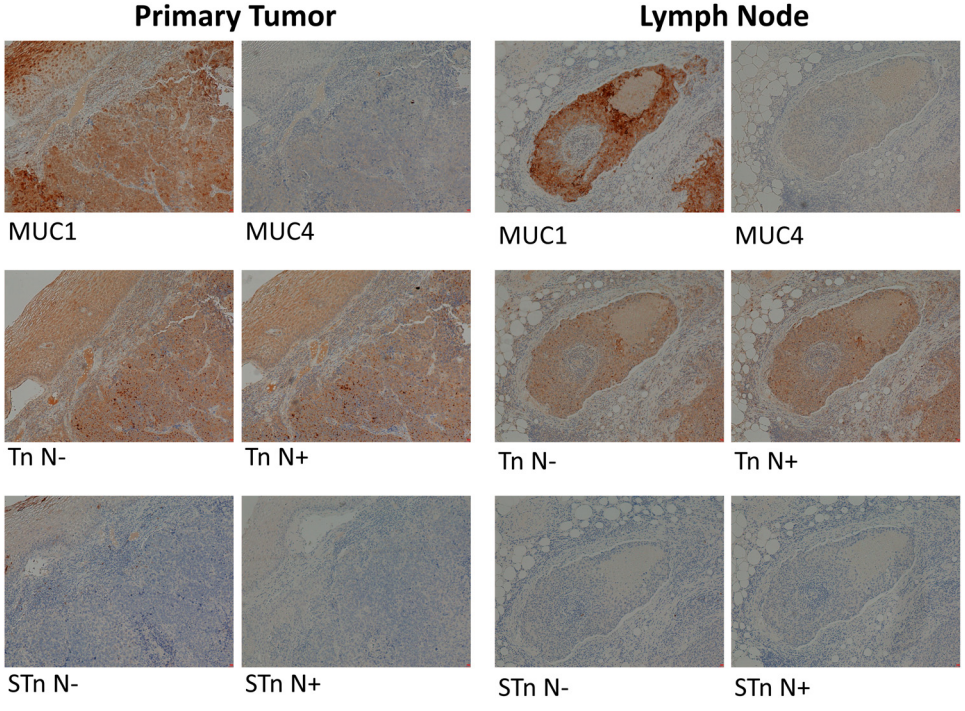

Fig. 1. Matching primary tumor and lymph node metastasis from one patient: MUC1 displays patchy strong (3+) cytoplasmic staining. Very minimal (0+) MUC4 staining is observed. Diffuse moderate (2+) staining is observed for Tn staining, with and without neuraminidase. Both the primary cervical tumor specimen and lymph node metastasis of squamous cell carcinoma of the cervix display negative (0+) staining for Sialyl Tn antigen with and without neuraminidase. All images were taken at 20X with 100 µM scale bar.

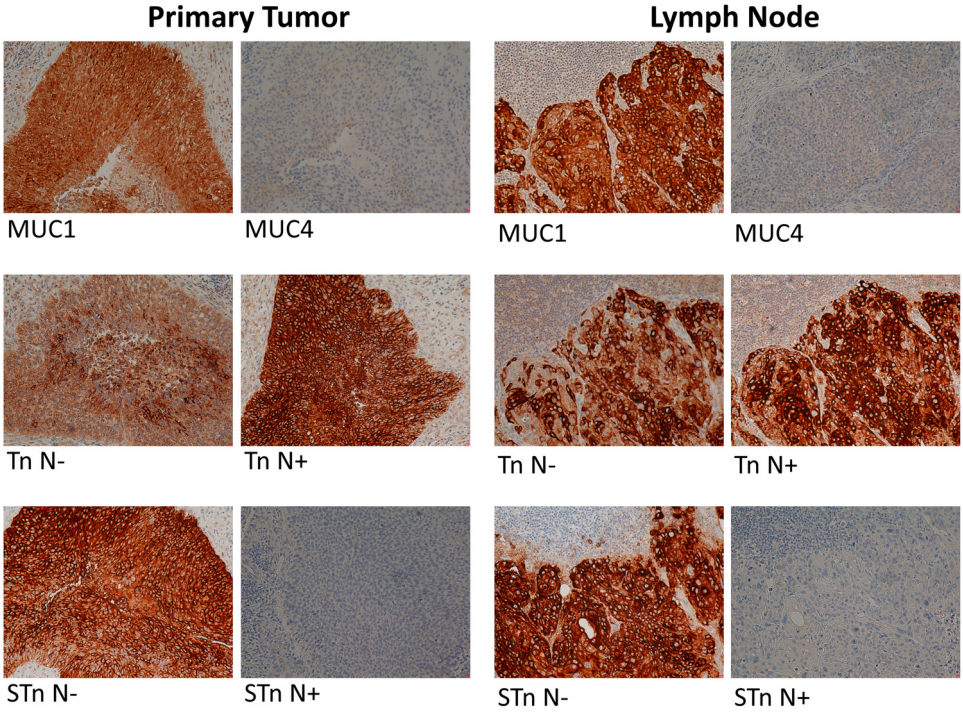

Fig. 2. Matching primary tumor and lymph node metastasis from a separate patient: Abnormal diffuse strong (3+) cytoplasmic MUC1 staining is observed. Very minimal (0+) MUC4 staining is observed. Both the primary cervical tumor specimen and lymph node metastasis of squamous cell carcinoma display diffuse strong (3+) cytoplasmic Tn antigen staining and Sialyl Tn antigen staining. Neuraminidase treatment results in loss of STn staining with a very slight decrease in Tn staining. All images were taken at 20X with 100 μM scale bar.

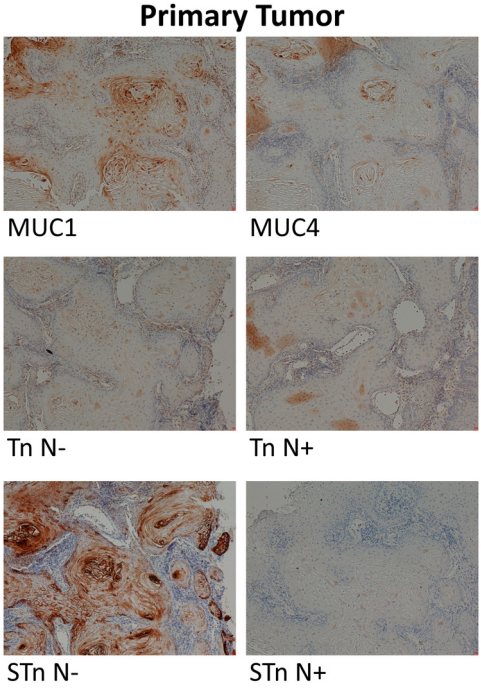

Fig. 3. Primary cervical well-differentiated keratinizing squamous cell carcinoma: In the innermost superficial cells, patchy moderate (2+) cytoplasmic staining is seen for Muc1, with very weak (1+) staining for MUC4 is observed. Very weak (0–1+) cytoplasmic staining is observed for Tn antigen, with and without neuraminidase. Patchy moderate-strong (2–3+), mostly membranous staining for STn antigen is observed which is lost with neuraminidase treatment. All images were taken at 20X with 100 μM scale bar.

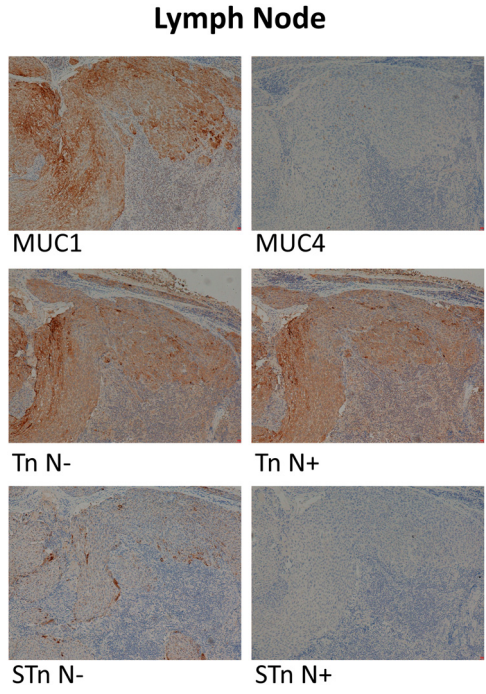

Fig. 4. A lymph node metastasis of squamous cell carcinoma of the cervix: Abnormal moderate (2+) cytoplasmic MUC1 staining is observed. Very minimal (0+) MUC4 staining is observed. Diffuse weak (1+) perinuclear dot-like Sialyl Tn antigen staining and diffuse moderate (2+) Tn antigen staining is observed. Neuraminidase treatment results in loss of STn staining but does not affect Tn staining. All images were taken at 20X with 100 µM scale bar.

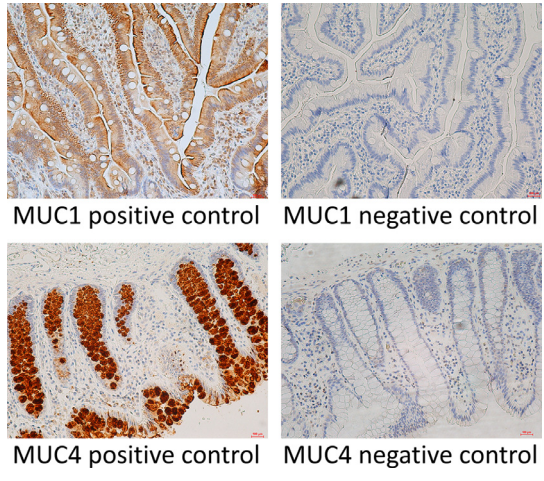

Fig. 5. Positive and negative control for MUC1 and MUC4: Human stomach with and without MUC1 antibody (1:100 dilution) demonstrating positive and negative control, respectively. Human colon tissue with and without MUC4 antibody (1:400 dilution) demonstrating positive and negative control, respectively.

3. Experimental Design, Materials and Methods

Prospectively collected and banked specimens from the clinical trial GOG 0221 (NCT00460356) were obtained with permission from the National Research Group (NRG) Oncology and National Cancer Institute (NCI). These formalin-fixed, paraffin-embedded specimens were derived from 139 patients >18 yrs of age with previously untreated stage IB-IVA (AJCC TNM staging system, 7th edition) primary cervical cancer, who underwent local surgical control with possible lymphadenectomy. The total number of specimens are as follows: 133 primary cervical cancer specimens, 28 para-aortic lymph node specimens, and 57 pelvic lymph node specimens (including the obturator, external iliac, and common iliac lymph nodes).

Sections from each specimen block underwent immunohistochemical staining using an automated tissue immunostainer *(Leica Bond-III Polymer Refine Detection System DS9800, Leica Biosystems, Deer Park, IL, USA)* and the following primary antibodies: **Tn** *(1:200 undiluted tissue culture supernatant, clone 5F4, mouse mAb IgM, H. Clausen / U. Mandel, Copenhagen Center for Glycomics, University of Copenhagen, Denmark)*, **Sialyl Tn** *(1:200 undiluted tissue culture supernatant, clone TKH2, mouse mAb IgG1, H. Clausen / U. Mandel, Copenhagen Center for Glycomics, University of Copenhagen, Denmark)*, **MUC1** *(dilution 1:100, clone HPA004279, rabbit pAb, Sigma-Aldrich, Inc., St. Louis, MO, USA)*, and **MUC4** *(dilution 1:400, clone HPA005895, rabbit pAb, Sigma-Aldrich, Inc., St. Louis, MO, USA)* [2]. The detailed staining process is as follows: initial deparaffinization and rehydration (on a Leica Multistainer, ST5020, Leica Biosystems, Deer Park, IL, USA); if applicable (for one Tn and STn slide each), treatment with 50 mU/mL neuramidase from *Arthrobacter ureafaciens* in 10 mM Tris–HCl, pH5.5 for 2.5 h in a humid chamber at 37 °C (10269611001; Roche, Indianapolis, IN); transfer of slides to the Leica Bond-III with target retrieval in a pH 6.0 citrate buffer for 20 min at 100 °C; incubation with 5% goat serum (01–6201, ThermoFisher Scientific, Waltham, MA, USA); application of peroxidase-blocking reagent; followed by primary antibody incubation for 60 min; subsequent secondary antibody incubation (post-primary IgG-linker and/or Poly-HRP IgG reagents); detection with 3,3′ diaminobenzidine tetrahydrochloride (DAB chromogen); counterstained with hematoxylin; subsequently dehydrated and mounted (Leica MM24 mounting media, Deer Park, USA).

Positive validation of biomarker staining was performed on sections of murine colon from T-synthase knockout mice (villin::Cre/floxed C1GalT1, Lijun Xia, Oklahoma Medical Research Foundation, Oklahoma City, OK); negative validation was performed on sections of murine colon from C57Bl/6J wild-type mice.

Evaluation of stained slides was performed by experienced gynecologic pathologists who were completely blinded to clinical parameters. The H-scores are provided in the companion *Gynecologic Oncology* article. To collate various tumor staining characteristics, an experienced gynecologic pathologist selected and photographed pertinent cases using a Nikon Eclipse Ni microscope (Minato City, Tokyo, Japan) utilizing NIS-Elements AR 3.2 64-bit software.

Ethics Statements

Relevant informed consent was obtained from subjects. The research was carried out in accordance with the Declaration of Helsinki and the University of Oklahoma Health Sciences Committee Institutional Board Review / Ethical committee (protocol number 8934).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

MUC1, MUC4, Stn, TN dataset in cervical cancer (Original data) (Mendeley Data).

CRediT Author Statement

Rajani Rai: Data curation, Writing – original draft, Writing – review & editing; **Rachel Conrad:** Data curation, Investigation, Writing – original draft; **Doris M. Benbrook:** Funding acquisition, Supervision, Conceptualization, Methodology, Writing – review & editing.

Acknowledgments

We thank Richard Cummings, PhD, for advice on glycoprotein biology used in the original design of the clinical trial, Hanke van der Wel and Christopher M. West, PhD, for their initial development of the immunohistochemical staining methods, and Sanam Hussain, MD for her review of the MUC1 and MUC4 H-scores provided in the companion article. Drs. Ullu Mandel and Henrik Clausen (Copenhagen) are thanked for generous gift of the monoclonal antibodies. and Ligjun Xia (Oklahoma Medical Research Foundation) for control samples from T-synthase mutant mice. This work was supported by the Gynecologic Cancer Program of the Stephenson Cancer Center, University of Oklahoma Health Sciences Center; and the National Cancer Institute Cancer Center [Grant P30CA225520]. Research reported in this publication was supported in part by the National Cancer Institute Cancer Center Support Grant P30CA225520 awarded to the University of Oklahoma Stephenson Cancer Center and used the Biospecimen and Tissue Pathology Shared Resource. This work was also supported by National Cancer Institute grants to NRG Oncology (U10 CA 180822) and NRG Operations (U10 CA180868). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Supplementary Materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dib.2023.109243.

References

[1] D.M. Benbrook, W. Deng, M.A. Gold, R. Rai, R. Conrad, H. van der Wel, S. Husain, K. Moore, N. Spirtos, A.L. Jackson, M. Zakhour, C.A. Mathews, C.M. West, Association of Sialyl Tn antigen with cervical cancer lymph node status: an NRG oncology/GOG study, Gynecol. Oncol. 171 (2023 Apr) 67–75, doi:10.1016/j.ygyno.2023.02.001.

[2] C. Steentoft, Z. Yang, S. Wang, et al., A validated collection of mouse monoclonal antibodies to human glycosyltransferases functioning in mucin-type O-glycosylation, Glycobiology 29 (2019) 645–656.