Differential Expression of MUC1, MUC2, and MUC5AC in Carcinomas of Various Sites

An Immunohistochemical Study

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Abstract

We studied immunohistochemical expression of MUC1, MUC2, and MUC5AC in 194 carcinomas of different primary sites to determine whether differential expression patterns could be used to distinguish different carcinomas. MUC1 was expressed by most (except adrenocortical and hepatocellular carcinomas). MUC2 was expressed infrequently (positive immunoreactivity primarily in tumors of gastrointestinal origin). MUC5AC was expressed by most pancreatic ductal and endocervical adenocarcinomas and a variable number of tumors of the gastrointestinal tract. A MUC1+/MUC2–/MUC5AC– immunophenotype was observed in most breast, lung, kidney, bladder, endometrial, and ovarian carcinomas; MUC1+/MUC2–/MUC5AC+ was characteristic of pancreatic ductal adenocarcinomas and cholangiocarcinomas. Adrenocortical and hepatocellular carcinomas were negative for all mucins. Carcinomas of gastrointestinal origin exhibited variable expression of each mucin examined and no consistent immunoreactivity pattern.

Many carcinomas can exhibit distinct MUC1, MUC2, and MUC5AC expression patterns, which might be valuable diagnostically in specific settings (eg, distinguishing cholangiocarcinoma from hepatocellular carcinoma or renal from adrenocortical carcinoma). However, the overlapping and heterogeneous patterns of MUC1, MUC2, and MUC5AC expression observed in many tumors, particularly those of gastrointestinal origin, preclude use of these markers in the routine immunohistochemical assessment of carcinomas of an unknown primary site.

Mucins are high-molecular-weight glycoproteins synthesized by a broad range of epithelial tissues. Structurally, mucin glycoproteins consist of a protein backbone with a large number of O-linked carbohydrate side chains. The protein backbone is composed of a variable number of tandem repeat regions rich in threonine and serine amino acid residues, the sequence and length of which are unique for each particular mucin.[1-5] Genes coding for the protein component of mucin are designated as MUCs. At present, 14 mucin glycoproteins have been assigned to the *MUC* gene family.[6] Mucins can be subdivided into membrane-associated and secreted forms.[3,4,7] MUC1 represents the best characterized membrane-associated mucin. The glycoprotein structure of MUC1 consists of an extracellular region composed of conserved tandem repeats of amino acids, a transmembrane domain, and a cytoplasmic tail.[2,3,8,9] Characteristic secretory mucins include MUC2 and MUC5AC, which structurally contain cysteine-rich regions and participate in the formation of extracellular gels.[10-12]

In normal tissues, mucins seem to be expressed in a relatively organ- and cell-specific manner.[10,13-15] Some mucins can be observed in several types of tissues, whereas others exhibit a more limited pattern of expression. For example, MUC1 is expressed on the apical surfaces of most epithelial cells, including those of the breast and the digestive, respiratory, and genitourinary tracts.[13,16,17] In contrast, the distribution of MUC2 and MUC5AC seems to be more restricted, with MUC2 specifically expressed in goblet cells of the small intestine and colon[13,14,18] and MUC5AC preferentially expressed in the stomach and respiratory tracts.[14,15,19-22] Although the characteristic patterns of mucin expression for each organ can be maintained during

neoplastic transformation, mucin expression sometimes is altered in carcinomas compared with normal tissues.[1,2,4,7,23] Nevertheless, this relative tissue specificity suggests that differential expression of particular mucins might be a useful means for discriminating between carcinomas of various sites and might have important applications in diagnostic surgical pathology.

The histologic distribution of mucins in tumors arising in various organs has been elucidated previously, with the majority of these studies focusing on the association of the expression of particular mucins with tumor progression, biologic behavior, and clinical prognosis.[7,23,24] Relatively few studies have examined the expression of specific mucins in the context of differentiating various types of carcinomas.[25-29] In the present study, we evaluated the expression of MUC1, MUC2, and MUC5AC in carcinomas of various organs by immunohistochemical methods. The objective of the present work was to determine the distribution pattern of these particular mucin glycoproteins in each type of carcinoma and to evaluate whether differential patterns of mucin expression could be used to distinguish tumors from different primary sites.

Materials and Methods

We obtained 194 cases of primary carcinoma from a variety of organs from the files of the Division of Pathology, City of Hope National Medical Center, Duarte, CA. Tissue samples from each of the cases were fixed in 10% neutral buffered formalin and embedded in paraffin. The sites of origin of the tumors are listed in **Table 1**. Histologic types of tumors examined included 10 adrenocortical carcinomas, 15 urothelial carcinomas of the bladder, 14 breast carcinomas (10 ductal, 3 lobular, 1 mucinous), 20 colonic adenocarcinomas (including 1 mucinous adenocarcinoma), 12 esophageal adenocarcinomas, 16 renal carcinomas (15 conventional/clear cell, 1 papillary), 13 hepatocellular carcinomas, 11 cholangiocarcinomas, 21 lung adenocarcinomas, 9 ovarian adenocarcinomas (7 serous, 1 endometrioid, 1 clear cell), 11 ductal adenocarcinomas of the pancreas, 11 prostatic adenocarcinomas, 12 gastric adenocarcinomas (including 1 mucinous adenocarcinoma), 9 endometrial adenocarcinomas, endometrioid type, and 10 endocervical adenocarcinomas.

Immunohistochemical staining was performed on formalin-fixed, paraffin-embedded sections using monoclonal antibodies directed against MUC1 (clone Ma695, dilution 1:100; Novocastra, Newcastle upon Tyne, England), MUC2 (clone Ccp58, dilution 1:100; Novocastra), and MUC5AC (clone CLH2, dilution 1:150; Novocastra) glycoproteins. Sections were deparaffinized in xylene and rehydrated in a graded ethanol series. Antigen retrieval was performed by steam heating slides in citrate buffer (pH 6.0) in a steamer (Black and Decker, Shelton, CT) for 20 minutes. Staining was performed using an automated immunostainer (DAKO, Carpinteria, CA), followed by antibody detection using the DAKO EnVision+ System and 3,3'-diaminobenzidine as a chromogen. The slides were counterstained with hematoxylin and coverslips applied. Appropriate positive and negative tissue control samples were used throughout. A particular tumor was considered positive if greater than 5% of the tumor cells reacted with any intensity.

Table 1
Frequencies of MUC1, MUC2, and MUC5AC Expression in Carcinomas of Various Organs

Organ	Tumor Type	No. of Cases	No. (%) of Positive Cases		
			MUC1	MUC2	MUC5AC
Adrenal	Cortical carcinoma	10	0 (0)	0 (0)	0 (0)
Bladder	Urothelial carcinoma	15	14 (93)	0 (0)	0 (0)
Breast	Ductal carcinoma	10	10 (100)	0 (0)	0 (0)
	Lobular carcinoma	3	3 (100)	0 (0)	0 (0)
	Mucinous carcinoma	1	1 (100)	1 (100)	0 (0)
Colon	Adenocarcinoma	19	10 (53)	12 (63)	5 (26)
	Mucinous adenocarcinoma	1	1 (100)	1 (100)	0 (0)
Esophagus	Adenocarcinoma	12	9 (75)	2 (17)	8 (67)
Kidney	Renal carcinoma	16	12 (75)	0 (0)	0 (0)
Liver	Hepatocellular carcinoma	13	0 (0)	0 (0)	0 (0)
	Cholangiocarcinoma	11	8 (73)	0 (0)	5 (45)
Lung	Adenocarcinoma	21	20 (95)	0 (0)	3 (14)
Ovary	Adenocarcinoma	9	9 (100)	1 (11)	0 (0)
Pancreas	Ductal adenocarcinoma	11	9 (82)	0 (0)	8 (73)
Prostate	Adenocarcinoma	11	4 (36)	0 (0)	0 (0)
Stomach	Adenocarcinoma	11	8 (73)	4 (36)	6 (55)
	Mucinous adenocarcinoma	1	0 (0)	1 (100)	1 (100)
Uterus	Endometrial adenocarcinoma	9	9 (100)	0 (0)	2 (22)
	Endocervical adenocarcinoma	10	8 (80)	0 (0)	7 (70)

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Results

MUC1

The majority of tumors examined were positive for MUC1 (Table 1). MUC1 immunoreactivity was characterized primarily by staining along the apical membranes of the tumor cells **Image 1**. This pattern of staining was observed predominantly in better-differentiated carcinomas; in less-differentiated tumors, membranous and/or cytoplasmic staining was present **Image 2**. MUC1-positive tumors included adenocarcinomas of the breast (14/14 [100%]), ovary (9/9 [100%]), endometrium (9/9 [100%]), lung (20/21 [95%]), and endocervix (8/10 [80%]) and carcinomas of the bladder (14/15 [93%]) and kidney (12/16 [75%]). MUC1 immunoreactivity also was frequently observed in tumors of the pancreaticobiliary tract, including 9 (82%) of 11 ductal adenocarcinomas of the pancreas and 8 (73%) of 11 cholangiocarcinomas. Among gastrointestinal tract neoplasms, MUC1 expression was present in 9 (75%) of 12 esophageal adenocarcinomas and 8 (67%) of 12 gastric adenocarcinomas. In contrast, only 11 (55%) of 20 colonic adenocarcinomas were positive for this marker. A relatively small percentage of cases of prostatic adenocarcinoma (4/11 [36%]) were positive for MUC1. Tumors consistently negative for MUC1 included adrenocortical and hepatocellular carcinomas.

MUC2

Most tumors were negative for MUC2 (Table 1). MUC2 expression was restricted primarily to tumors of the gastrointestinal tract with positive immunoreactivity noted in 13 (65%) of 20 colonic adenocarcinomas **Image 3**, 5 (42%) of 12 gastric adenocarcinomas, and 2 (17%) of 12 esophageal adenocarcinomas. A cytoplasmic staining pattern was observed. Only rare tumors outside the gastrointestinal tract were observed to be positive for MUC2 and included a mucinous carcinoma of the breast **Image 4** and a clear cell–type adenocarcinoma of the ovary.

MUC5AC

Similar to MUC2, MUC5AC exhibited a cytoplasmic pattern of immunoreactivity. Expression of MUC5AC was noted primarily in tumors of gastrointestinal, pancreaticobiliary, and endocervical origin (Table 1). Most cases of adenocarcinoma of the esophagus (8/12 [67%]) and stomach (7/12 [58%]) were positive, whereas only a subset of colonic adenocarcinomas (5/20 [25%]) were positive for this marker. MUC5AC immunoreactivity also was noted in 8 (73%) of 11 pancreatic ductal adenocarcinomas **Image 5A** and 5 (45%) of 11 cholangiocarcinomas. The majority (7/10 [70%]) of endocervical adenocarcinomas exhibited MUC5AC positivity **Image 5B**. Other tumors occasionally exhibiting MUC5AC expression included adenocarcinomas of the endometrium (2/9 [22%]) and lung (3/21 [14%]). All other neoplasms examined were negative for MUC5AC.

MUC1, MUC2, and MUC5AC Expression Patterns

The MUC expression patterns observed in the various tumors studied are summarized in **Table 2** and **Table 3**. A MUC1+/MUC2–/MUC5AC– expression pattern was noted in a number of tumors and was particularly characteristic of ductal and lobular carcinomas of the breast (13/13 [100%]),

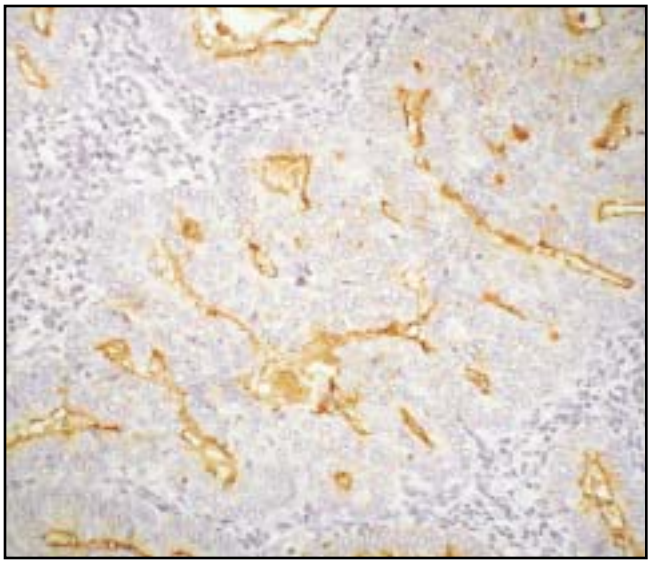

Image 1 Apical membrane MUC1 expression in endometrial adenocarcinoma (original magnification ×200).

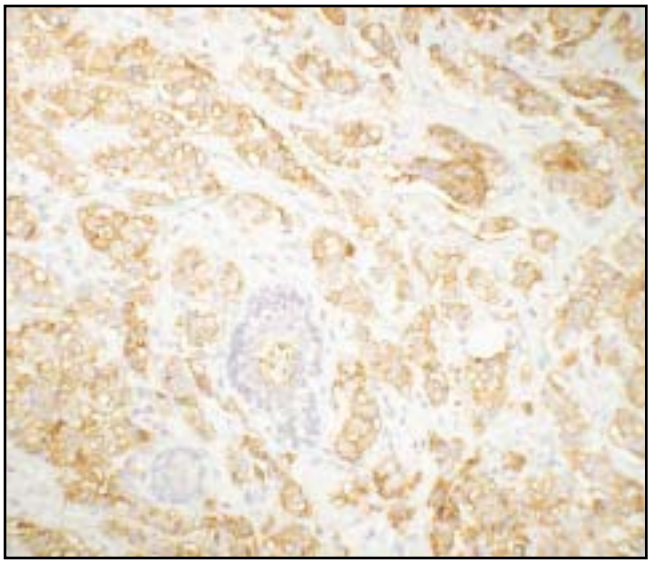

Image 2 Membranous and cytoplasmic MUC1 immunoreactivity in ductal carcinoma of the breast (original magnification ×100).

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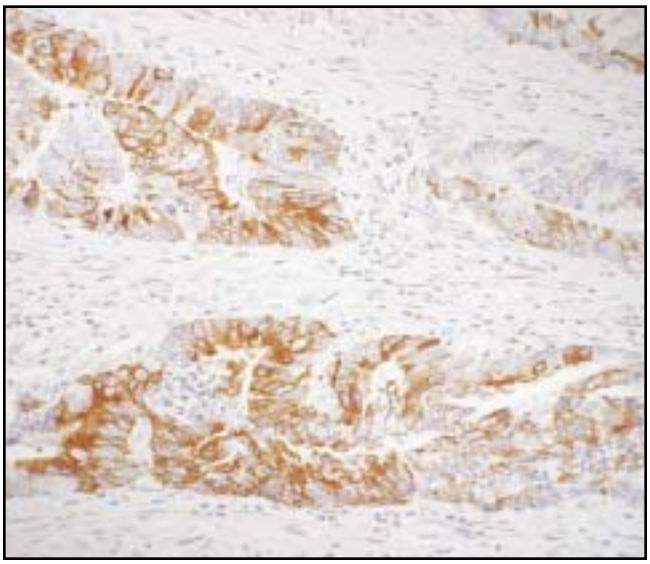

Image 3 Cytoplasmic MUC2 immunoreactivity in colonic adenocarcinoma (original magnification ×200).

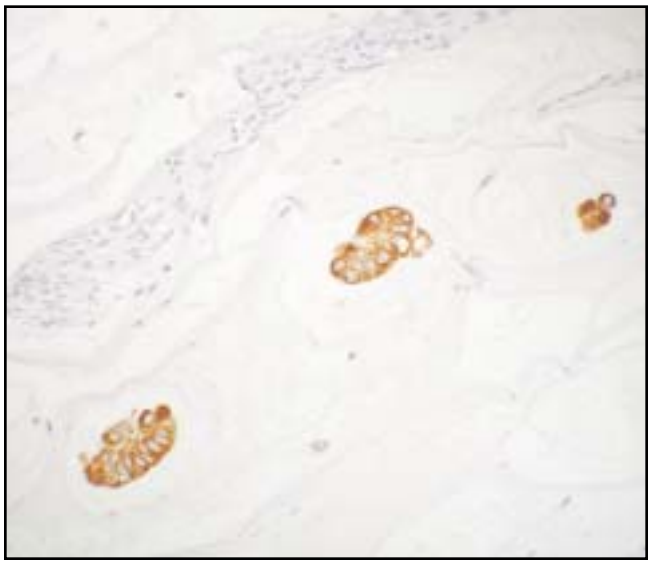

Image 4 MUC2 expression in mucinous carcinoma of the breast (original magnification ×200).

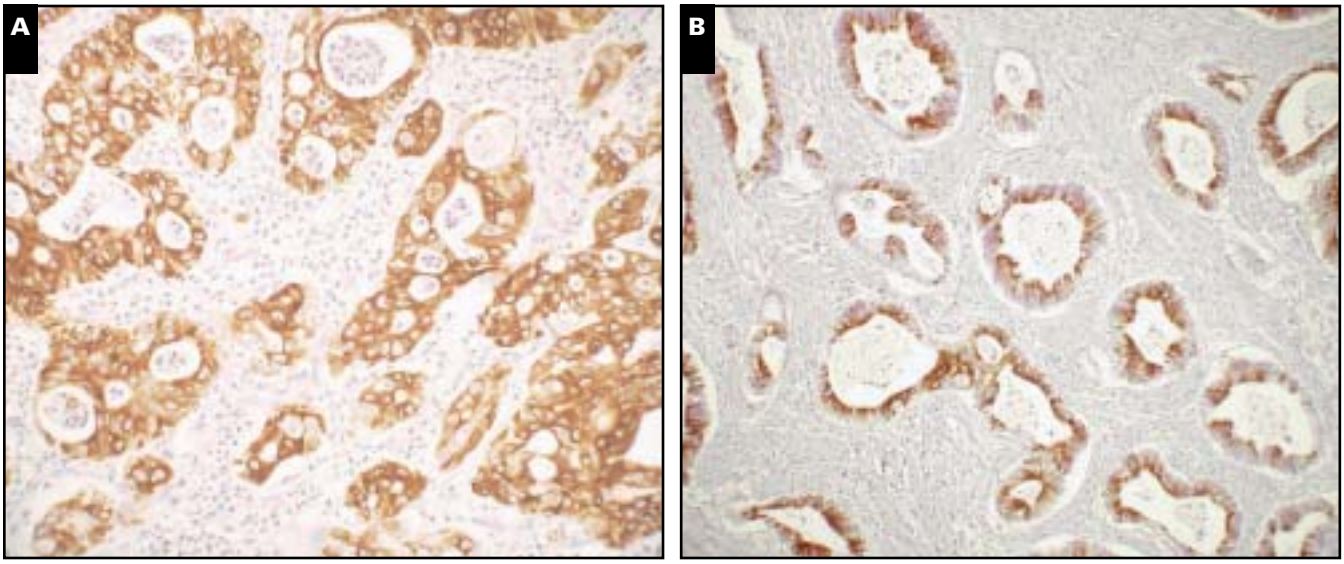

Image 5 Cytoplasmic MUC5AC immunoreactivity in pancreatic ductal adenocarcinoma (**A**, original magnification ×200) and endocervical adenocarcinoma (**B**, original magnification ×100).

urothelial carcinomas of the bladder (14/15 [93%]), and renal carcinomas (12/16 [75%]). This expression pattern also was observed in the majority of ovarian adenocarcinomas of various histologic subtypes. The majority of pulmonary (17/21 [81%]) and endometrial (7/9 [78%]) adenocarcinomas also were observed to be MUC1+/MUC2–/MUC5AC–; however, a small subset of these tumors expressed MUC5AC as well. A MUC1+/MUC2–/MUC5AC+ staining pattern was observed most often in ductal adenocarcinomas of the pancreas (7/11 [64%]) in addition to 5 (50%) of the 10 endocervical adenocarcinomas studied. Tumors of the gastrointestinal tract (esophagus, stomach, and colon), exhibited variable expression of each of the MUC glycoproteins studied, with no consistent pattern of immunoreactivity observed (Table 3). Tumors notably negative for MUC1, MUC2, and MUC5AC included adrenocortical carcinomas, hepatocellular carcinomas, and the majority of prostatic adenocarcinomas.

Discussion

In normal tissues, mucins seem to exhibit tissue- and cell-specific patterns of expression. The patterns of distribution exhibited might be quite complex, with several different

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Table 2
Expression Profiles of MUC1, MUC2, and MUC5AC in Nongastrointestinal Carcinomas*

MUC1/MUC2/MUC5AC Profile	Adrenal Cortical Carcinoma (n = 10)	Bladder Urothelial Carcinoma (n = 15)	Breast Ductal Carcinoma (n = 10)	Breast Lobular Carcinoma (n = 3)	Breast Mucinous Carcinoma (n = 1)	Renal Carcinoma (n = 16)	Lung Adeno-carcinoma (n = 21)	Ovary Adeno-carcinoma (n = 9)	Prostate Adeno-carcinoma (n = 11)	Endometrial Adeno-carcinoma (n = 9)	Endocervical Adeno-carcinoma (n = 10)
MUC1+/MUC2+/MUC5AC+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
MUC1+/MUC2+/MUC5AC–	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
MUC1+/MUC2–/MUC5AC–	0 (0)	14 (93)	10 (100)	3 (100)	0 (0)	12 (75)	17 (81)	8 (89)	4 (36)	7 (78)	3 (30)
MUC1+/MUC2–/MUC5AC+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (14)	0 (0)	0 (0)	2 (22)	5 (50)
MUC1–/MUC2+/MUC5AC+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
MUC1–/MUC2+/MUC5AC–	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
MUC1–/MUC2–/MUC5AC+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)
MUC1–/MUC2–/MUC5AC–	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	4 (25)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)

* Data are given as number (percentage) of positive cases.

Table 3
Expression Profiles of MUC1, MUC2, and MUC5AC in Carcinomas of the Gastrointestinal Tract*

MUC1/MUC2/MUC5AC Profile	Colon Adeno-carcinoma (n = 19)	Colon Mucinous Adeno-carcinoma (n = 1)	Esophagus Adeno-carcinoma (n = 12)	Hepatocellular Carcinoma (n = 13)	Liver Cholangio-carcinoma (n = 11)	Pancreas Ductal Adeno-carcinoma (n = 11)	Stomach Adeno-carcinoma (n = 11)	Stomach Mucinous Adenocarcinoma (n = 1)
MUC1+/MUC2+/MUC5AC+	3 (16)	0 (0)	2 (17)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)
MUC1+/MUC2+/MUC5AC–	2 (11)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)
MUC1+/MUC2–/MUC5AC–	5 (26)	0 (0)	2 (17)	0 (0)	3 (27)	2 (18)	2 (18)	0 (0)
MUC1+/MUC2–/MUC5AC+	0 (0)	0 (0)	5 (42)	0 (0)	5 (45)	7 (64)	3 (27)	0 (0)
MUC1–/MUC2+/MUC5AC+	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)
MUC1–/MUC2+/MUC5AC–	6 (32)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)
MUC1–/MUC2–/MUC5AC+	1 (5)	0 (0)	1 (8)	0 (0)	0 (0)	1 (9)	1 (9)	0 (0)
MUC1–/MUC2–/MUC5AC–	1 (5)	0 (0)	2 (17)	0 (0)	3 (27)	1 (9)	1 (9)	0 (0)

* Data are given as number (percentage) of positive cases.

mucins often expressed in the same organ and, at times, the same cell.[13,19-21] However, the distinct expression patterns observed in normal tissues can be modified under pathologic conditions. In carcinomas, dysregulation of mucin expression can occur, including increased, loss of, and aberrant expression of various mucin glycoproteins.[1,2,4,7,23] Many studies have defined the patterns of mucin expression in carcinomas of different organs; however, few have emphasized analysis of differential mucin expression patterns as potential discrimination markers among tumors.[25-29]

In the present study, a number of tumors were observed to exhibit consistent MUC1 immunoreactivity, including carcinomas of the breast, lung, endometrium, endocervix, ovary, bladder, kidney, esophagus, stomach, pancreas, and bile duct. These results are consistent with the findings of previous studies[2,7,13,15,23,24,30-37] and are thought to reflect the wide distribution of MUC1 expression in normal tissues.

In contrast with MUC1, MUC2 expression was noted predominantly in tumors of the gastrointestinal tract, including carcinomas of colonic, gastric, and esophageal origin. However, MUC2 immunoreactivity was observed in only 65% of the colon carcinomas (13/20) and fewer than half of the gastric and esophageal carcinomas, in accordance with results reported in the literature,[2,7,13,38-51] which somewhat limits the use of MUC2 as a sensitive marker of tumors of these particular sites. In addition, MUC2 might not be entirely specific for gastrointestinal tumors; previous studies have indicated that MUC2 positivity can be found regularly in a high percentage of carcinomas with predominantly mucinous features, regardless of the site of origin, including those arising from the ovary, breast, and pancreas.[26,52-56] The majority of tumors examined in this study were nonmucinous; however, all mucinous carcinomas that were studied (1 each from the breast, stomach, and colon) were positive for MUC2, which would seem to be consistent with these previous observations.

Similar to previous studies,[2,15,22,24,32,44,46,48-50,57-64] MUC5AC immunoreactivity was observed in a variable percentage of carcinomas of pancreaticobiliary, gastrointestinal, and endocervical origin in the present study, with the highest percentage of positive cases noted in ductal adenocarcinomas of the pancreas, esophageal adenocarcinomas, and endocervical adenocarcinomas. In contrast, carcinomas from other sites examined seldom were positive for MUC5AC. This observed differential expression of MUC5AC suggests that this particular mucin glycoprotein

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might prove to be a useful marker for separating carcinomas of the digestive system from other types of adenocarcinomas or for distinguishing endocervical from endometrial adenocarcinomas. It should be recognized, however, that the specificity of MUC5AC expression in these particular settings is not absolute, because MUC5AC positivity also was noted in a small percentage of lung and endometrial adenocarcinomas in the present study. A similar rate of MUC5AC expression in pulmonary adenocarcinomas has been observed.[65] In addition, while no MUC5AC-positive breast carcinomas were noted in the present study, a small percentage of ductal carcinomas of the breast have been observed to be positive by other investigators.[56,66]

Through examination of coordinate expression of MUC1, MUC2, and MUC5AC, the present study demonstrates particular differential expression patterns characteristic of various carcinomas that might be of discriminative value and permit, in the proper context, identification of carcinomas of certain types. For example, a MUC1+/MUC2–/MUC5AC– immunophenotype was observed in the majority of carcinomas of the breast, lung, kidney, bladder, endometrium, and ovary, whereas a MUC1+/MUC2–/MUC5AC+ pattern was particularly characteristic of ductal adenocarcinomas of the pancreas and a number of cases of cholangiocarcinoma. A subset of tumors were consistently negative for all mucins studied (MUC1–/MUC2–/MUC5AC–) and included adrenocortical carcinomas and hepatocellular carcinomas. These results suggest several possible situations in which mucin immunophenotyping might be useful, including differentiating hepatocellular carcinoma (MUC1–/MUC2–/MUC5AC–) from cholangiocarcinoma (MUC1+/MUC2–/MUC5AC+) and distinguishing renal (MUC1+/MUC2–/MUC5AC–) from adrenocortical (MUC1–/MUC2–/MUC5AC–) carcinomas. Differential expression of MUC1, MUC2, and MUC5AC might be used as an adjunct to other immunohistochemical markers typically used in these diagnostic settings.[67-70] Additional studies are required to confirm the diagnostic usefulness and relative effectiveness of analyzing mucin glycoprotein expression patterns in these differential diagnostic situations.

Several other investigators also have highlighted the usefulness of the differential expression of mucin glycoproteins in specific diagnostic settings.[25-29] For example, in a study addressing primary signet-ring cell carcinomas of the lung, Hayashi et al[25] demonstrated these particular tumors to be positive for MUC1 and negative for MUC2, in contrast with signet-ring cell carcinomas of the stomach and colon, which generally were negative for MUC1 and positive for MUC2. Based on these observations, MUC1 and MUC2 immunohistochemical analysis was suggested as a useful means of distinguishing primary and metastatic signet-ring cell carcinomas. MUC2 expression also has been used in the differential diagnosis of ovarian tumors. O'Connell et al[27,28] demonstrated consistent MUC2 expression in cases of mucinous tumors of the appendix and pseudomyxoma peritonei but not in primary ovarian mucinous tumors, suggesting that MUC2 can be used to distinguish pseudomyxoma peritonei secondarily involving the ovary from primary ovarian mucinous tumors with peritoneal implants.

Differential expression of MUC2, along with MUC5AC, also has been found to be of value in the context of discriminating primary ovarian carcinoma and colonic carcinoma metastatic to the ovary.[26] In this particular study, Albarracin et al[26] observed metastatic colon carcinomas to be positive for MUC2 and negative for MUC5AC, whereas most primary ovarian endometrioid-type carcinomas were mostly negative for MUC2 and positive for MUC5AC, and primary ovarian mucinous cystadenocarcinomas generally were positive for both markers. Based on these findings, the authors concluded that differential immunohistochemical expression of MUC2 and MUC5AC was useful for distinguishing metastatic colon carcinoma involving the ovary and primary ovarian mucinous or endometrioid carcinomas. More recently, Lee et al,[29] in an immunohistochemical study using tissue microarray technology, were able to classify and separate various carcinomas of the digestive tract based on the expression patterns of different mucins and cytokeratins. Specifically, MUC1 and MUC5AC, along with cytokeratins 7, 13, 19, and 20, were found to be the most useful markers for discriminating among the various neoplasms in their particular study.

While the results of the present study and those of previous investigations[25-29] suggest a role for mucin immunohistochemical analysis in the differential diagnosis of specific types of carcinomas in particular clinical settings, in the context of evaluation of carcinomas from an unknown primary site, the diagnostic usefulness of mucin expression patterns seems somewhat limited. Although many carcinomas in the present study could be characterized by a particular expression profile with respect to MUC1, MUC2, and MUC5AC immunoreactivity, several common tumors, particularly of gastrointestinal origin, exhibited variable and heterogeneous mucin phenotypes, many of which overlapped with those of other carcinomas. For example, while many nongastrointestinal adenocarcinomas, such as those of the breast and lung, exhibited predominantly a MUC1+/MUC2–/MUC5AC– immunophenotype, this particular pattern of mucin expression also was observed in a number of adenocarcinomas of the gastrointestinal tract, including those of colonic (5/20 [25%]), gastric (2/12 [17%]), and esophageal (2/12 [17%]) origin. Heterogeneous mucin expression patterns exhibited by carcinomas arising in the gastrointestinal tract also have been observed by other investigators.[2,7,15,23,46-50,57,60]

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The overlapping patterns of MUC1, MUC2, and MUC5AC expression seen in many tumors suggests that the use of these particular antibodies has low discriminative value for determining the primary site of carcinomas manifesting as metastatic disease. While the carcinomas evaluated in the present study all were primary tumors, metastatic carcinomas would be expected to retain MUC expression patterns similar to those of their corresponding primary sites of origin. However, further studies are required to confirm this assumption.

The present comprehensive study documents the expression of MUC1, MUC2, and MUC5AC in carcinomas arising in a number of different primary sites. The results indicate that many carcinomas might exhibit distinct expression patterns of these particular mucin glycoproteins. Differential expression of MUC1, MUC2, and MUC5AC might be of value in specific diagnostic settings, such as separating hepatocellular carcinoma and cholangiocarcinoma and distinguishing adrenocortical from renal carcinomas. The immunohistochemical analysis of mucin expression patterns seems to be a promising means of improving diagnostic accuracy in these particular settings. However, use of these markers seems to have a limited role in the immunohistochemical evaluation of carcinomas of unknown origin, primarily owing to the overlapping patterns of MUC1, MUC2, and MUC5AC expression exhibited by many tumors.

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