

GATA3 expression analysis in tissue microarrays of 13,204 samples from 135 human tumor types.

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Introduction and Objectives

GATA Binding Protein 3 (GATA3) is a transcription factor with key importance for the differentiation of the breast and urothelium. Accordingly, in surgical pathology, GATA3 is commonly used as a diagnostic marker for these tissues. However, GATA3 may also become expressed in neoplasms originating from other tissues.

To evaluate GATA3 expression tumor tissues, we analyzed a tissue microarray containing 16,611 samples from 133 different tumor types by means of immunohistochemistry.

Materials & Methods

Tissue Microarrays (TMAs). The normal tissue TMA was composed of 8 samples from 8 different donors for each of 76 different normal tissue types (608 samples on one slide). The cancer TMAs contained a total of 16,611 primary tumors from 133 tumor types and subtypes.



Normal tissue TMA

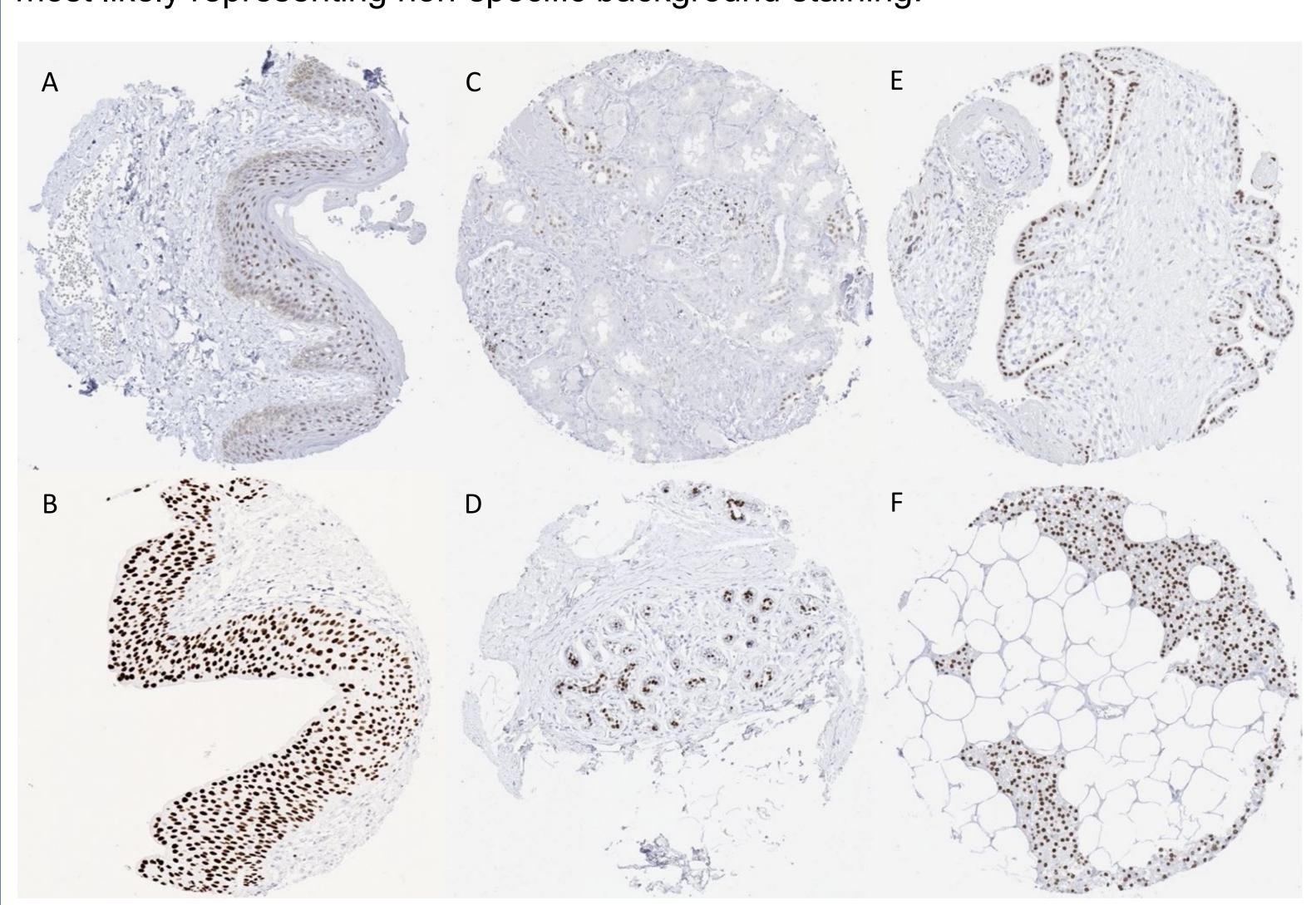
Multitumor TMA (total: 43 slides)

Immunostaining protocol and controls

- Antibody: MS validated antibodies, clone MSVA-450M, Mouse IgG, Dilution: 1:50
- Antigen retrieval: 5 min at 121°C (autoclave) in pH 7.8 buffer
- Controls:
- Kidney: Moderate to strong nuclear staining reaction should be seen in a fraction of collecting duct cells and podocytes in glomeruli. Staining should be absent in proximal and distal tubuli as well as in blood vessels.
- Tonsil: Most T helper cells should show weak to moderate nuclear staining, whereas staining should be absent in B-cells.

GATA3 in normal tissues

Nuclear GATA3 immunostaining was seen in urothelium (+++), squamous epithelium of the skin (+++; superficial cell layers >basal cell layers), hair follicles (+++), sebaceous glands (++), parathyroid gland (+++), trophoblastic cells (+ -+++; more intense in first than in the third trimenon), chorion cells (+++), and amnion cells (+) of the placenta, collecting ducts (+++; not all) and glomerular podocytes (++) of the kidney, seminal vesicle epithelium (+++), tall columnar cells and basal cells (++) of the epididymis, a fraction of the luminal cells of breast glands (+++), basal cells in the prostate (+; not always visible), glandular cells (especially mucinous) of salivary glands (+ - ++), and a fraction of lymphocytes, most prominently in the thymus (++). A faint cytoplasmic GATA3 staining was seen in gastric glands and goblet cells of respiratory epithelium, most likely representing non-specific background staining.



GATA3 immunostaining of normal tissues. The panels show a strong nuclear GATA3 positivity of predominantly suprabasal cells in the epidermis of the skin (A), urothelial cells of all layers (B), podocytes and collecting duct cells of the kidney (C) luminal cells of the breast (D), trophoblastic cells of the placenta (E) and epithelial cells of the parathyroid gland (F).

Conclusions

- GATA3 expression can occur in various tumor entities including breast, urothelial, salivary gland, squamous cell and other tumors.
- Particularly high frequency and levels of GATA3 occur in breast and urothelial carcinoma.
- A reduced level of GATA3 reflects cancer progression and poor patient prognosis in these tumor entities.

GATA3 in tumor tissues

Seventy (53%) of 133 tumor categories showed detectable GATA3 expression with 24 (18%) tumor categories including at least one case with strong positivity. The highest rate of positive staining and the highest levels of expression was found in various subtypes of breast and urinary bladder neoplasms as well as in basal cell carcinoma of the skin. At lower frequency and often at lower intensity, GATA3 immunostaining could be seen in various categories of salivary gland tumors, neuroendocrine tumors as well as in squamous cell carcinomas or tumors containing squamous cell elements such as endometroid carcinomas.

		GATA3 immunostaining						
	Tumor entity	on TMA (n)	interpr. (n)	neg. (%)	weak (%)	mod. (%)	strong (%)	
Tumors of the skin	Pilomatrixoma	35	31	100.0	0.0	0.0	0.0	
	Basal cell carcinoma	88	68	2.9	11.8	47.1	38.2	
	Benign nevus	29	22	100.0	0.0	0.0	0.0	
	Squamous cell carcinoma of the skin	90	77	84.4	14.3	0.0	1.3	
	Malignant melanoma	46	38	97.4	2.6	0.0	0.0	
T and af the beard	Merkel cell carcinoma	46	40	100.0	0.0	0.0	0.0	
Tumors of the head and neck	- 4	109	103	98.1	1.9	0.0	0.0	
and neck	Squamous cell carcinoma of the pharynx Oral squamous cell carcinoma (floor of the mouth)	60 130	59 127	100.0 93.7	0.0 3.9	0.0 1.6	0.0	
	Pleomorphic adenoma of the parotid gland	50	46	100.0	0.0	0.0	0.0	
	Warthin tumor of the parotid gland	104	96	100.0	0.0	0.0	0.0	
	Adenocarcinoma, NOS (Papillary Cystadenocarcinoma)	14	12	66.7	8.3	25.0	0.0	
	Salivary duct carcinoma	15	11	72.7	18.2	9.1	0.0	
	Acinic cell carcinoma of the salivary gland	181	142	96.5	2.8	0.7	0.0	
	Adenocarcinoma NOS of the salivary gland	109	77	84.4	9.1	1.3	5.2	
	Adenoid cystic carcinoma of the salivary gland	180	104	95.2	3.8	1.0	0.0	
	Basal cell adenocarcinoma of the salivary gland	25	21	95.2	0.0	4.8	0.0	
	Basal cell adenoma of the salivary gland	101	88	100.0	0.0	0.0	0.0	
	Epithelial-myoepithelial carcinoma of the salivary gland	53	50	76.0	12.0	12.0	0.0	
	Mucoepidermoid carcinoma of the salivary gland	343	257	93.0	4.3	1.2	1.6	
	Myoepithelial carcinoma of the salivary gland	21	19	84.2	5.3	10.5	0.0	
	Myoepithelioma of the salivary gland	11	8	87.5	0.0	12.5	0.0	
	Oncocytic carcinoma of the salivary gland	12	12	91.7	8.3	0.0	0.0	
	Polymorphous adenocarcinoma, low grade, of the salivary gland	41	31	100.0	0.0	0.0	0.0	
	Pleomorphic adenoma of the salivary gland	53	36	94.4	5.6	0.0	0.0	
Tumors of the lung,	Adenocarcinoma of the lung	196	138	99.3	0.0	0.0	0.7	
pleura and thymus	Squamous cell carcinoma of the lung	80	50	98.0	2.0	0.0	0.0	
	Small cell carcinoma of the lung	16	11	100.0	0.0	0.0	0.0	
	Mesothelioma, epitheloid	39	30	93.3	6.7	0.0	0.0	
	Mesothelioma, other types	76	54	83.3	11.1	5.6	0.0	
	Thymoma	29	26	100.0	0.0	0.0	0.0	
Tumors of the	Squamous cell carcinoma of the vagina	78	55	94.5	3.6	1.8	0.0	
female genital tract	Squamous cell carcinoma of the vulva	130	118	94.9	5.1	0.0	0.0	
	Squamous cell carcinoma of the cervix	128	119	91.6	5.9	1.7	0.8	
	Endometrioid endometrial carcinoma	236	222	99.5	0.5	0.0	0.0	
	Endometrial serous carcinoma	82	66	100.0	0.0	0.0	0.0	
	Carcinosarcoma of the uterus	48	38	100.0	0.0	0.0	0.0	
	Endometrial carcinoma, high grade, G3 Endometrial clear cell carcinoma	13	13 7	100.0	0.0	0.0	0.0	
		8 110	7	100.0 95.1	0.0	0.0	0.0 2.4	
	Endometrioid carcinoma of the ovary Serous carcinoma of the ovary	559	82 443	99.8	2.4 0.2	0.0 0.0	0.0	
	Mucinous carcinoma of the ovary	96	62	100.0	0.2	0.0	0.0	
	Clear cell carcinoma of the ovary	50 50	37	100.0	0.0	0.0	0.0	
	Carcinosarcoma of the ovary	47	36	91.7	8.3	0.0	0.0	
	Brenner tumor	9	9	55.6	0.0	44.4	0.0	
Tumors of the	Invasive breast carcinoma of no special type	1345	1137	7.7	3.6	4.9	83.8	
breast	Lobular carcinoma of the breast	293	232	1.7	3.4	9.1	85.8	
	Medullary carcinoma of the breast	26	26	57.7	7.7	15.4	19.2	
	Tubular carcinoma of the breast	27	22	0.0	9.1	18.2	72.7	
	Mucinous carcinoma of the breast	58	42	4.8	4.8	4.8	85.7	
	Phyllodes tumor of the breast	50	42	11.9	7.1	14.3	66.7	
Tumors of the	Adenomatous polyp, low-grade dysplasia	50	46	100.0	0.0	0.0	0.0	
digestive system	Adenomatous polyp, high-grade dysplasia	50	46	100.0	0.0	0.0	0.0	
	Adenocarcinoma of the colon	1882	1587	100.0	0.0	0.0	0.0	
	Gastric adenocarcinoma, diffuse type	176	145	99.3	0.7	0.0	0.0	
	Gastric adenocarcinoma, intestinal type	174	137	99.3	0.7	0.0	0.0	
	Gastric adenocarcinoma, mixed type	62	56	100.0	0.0	0.0	0.0	
	Adenocarcinoma of the esophagus	83	51	100.0	0.0	0.0	0.0	
	Squamous cell carcinoma of the esophagus	76	33	97.0	3.0	0.0	0.0	
	Squamous cell carcinoma of the anal canal	89	80	92.5	3.8	3.8	0.0	
	Cholangiocarcinoma	113	105	100.0	0.0	0.0	0.0	
	Hepatocellular carcinoma	50	50	100.0	0.0	0.0	0.0	
	Ductal adenocarcinoma of the pancreas	612	430	97.2	1.9	0.9	0.0	
	Pancreatic/Ampullary adenocarcinoma	89	71	100.0	0.0	0.0	0.0	
	Acinar cell carcinoma of the pancreas	16	14	100.0	0.0	0.0	0.0	
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2.6	0.0	0.0	
0.0			
	0.0	0.0	
1.9	0.0	0.0	
0.0	0.0	0.0	
3.9	1.6	8.0	
0.0	0.0	0.0	
0.0	0.0	0.0	
8.3	25.0	0.0	Tumors of the
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2.8	0.7	0.0	
9.1	1.3	5.2	
3.8	1.0	0.0	
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12.0	12.0	0.0	
4.3	1.2	1.6	
5.3	10.5	0.0	
			Tumors of
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8.3	0.0	0.0	endocrine o
0.0	0.0	0.0	
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0.0	0.0	0.7	
2.0	0.0	0.0	
0.0	0.0	0.0	
6.7	0.0	0.0	
11.1	5.6	0.0	
0.0	0.0	0.0	
3.6	1.8	0.0	
5.1	0.0	0.0	
5.9	1.7	8.0	
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0.0	0.0	0.0	
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2.4	0.0	2.4	lymphoid tis
0.2	0.0	0.0	•
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8.3	0.0	0.0	
0.0	44.4	0.0	
3.6	4.9	83.8	
3.4	9.1	85.8	Tumors of s
7.7	15.4	19.2	tissue and b
9.1	18.2	72.7	
4.8	4.8	85.7	
7.1	14.3	66.7	
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0.7	0.0	0.0	
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3.0	0.0	0.0	
3.8	3.8	0.0	
0.0	0.0	0.0	
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1.9	0.9	0.0	
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result		Lov
strong (%)	P	adv
		spe
88.3	0.032	
83.8		
73.5		
98.2	<0.0001	
91.2		
68.6		
85.3	0.9688	
85.0		
83.3		
78.6		
84.9	0.0085	
70.0		

121 44.6 18.2 16.5 20.7

		GATA3 immunostaining						
	Tumor entity	on TMA (n)	interpr. (n)	neg. (%)	weak (%)	mod. (%)	stro (%	
Tumors of the	Non-invasive papillary urothelial carcinoma, pTa G2 low grade	177	147	0.0	0.0	0.7	99	
urinary system	Non-invasive papillary urothelial carcinoma, pTa G2 high grade	141	117	0.0	0.0	1.7	98	
	Non-invasive papillary urothelial carcinoma, pTa G3	187	161	3.7	0.6	3.1	92	
	Urothelial carcinoma, pT2-4 G3	1206	603	26.9	13.1	15.1	44	
	Small cell neuroendocrine carcinoma of the bladder	20	19	94.7	0.0	0.0	5.	
	Sarcomatoid urothelial carcinoma	25 957	20 570	60.0	5.0	10.0	25	
	Clear cell renal cell carcinoma	857 255	578 161	99.3 97.5	0.2 0.0	0.5 2.5	0. 0.	
	Papillary renal cell carcinoma Clear cell (tubulo) papillary renal cell carcinoma	233 21	15	93.3	6.7	0.0	0.	
	Chromophobe renal cell carcinoma	131	93	94.6	2.2	3.2	0.	
	Oncocytoma	177	114	99.1	0.0	0.9	0.	
Tumors of the male	Adenocarcinoma of the prostate, Gleason 3+3	83	79	100.0	0.0	0.0	0.	
genital organs	Adenocarcinoma of the prostate, Gleason 4+4	80	67	98.5	0.0	1.5	0.	
	Adenocarcinoma of the prostate, Gleason 5+5	85	77	100.0	0.0	0.0	0.	
	Adenocarcinoma of the prostate (recurrence)	258	175	97.7	2.3	0.0	0	
	Small cell neuroendocrine carcinoma of the prostate	19	15	93.3	6.7	0.0	0	
	Seminoma	621	608	99.8	0.0	0.2	0	
	Embryonal carcinoma of the testis	50	30	100.0	0.0	0.0	0	
	Yolk sac tumor	50	31	67.7	29.0	3.2	0	
	Teratoma	50	39	84.6	10.3	5.1	0	
	Squamous cell carcinoma of the penis	80	79	92.4	6.3	0.0	1	
Tumors of	Adenoma of the thyroid gland	113	103	100.0	0.0	0.0	0	
endocrine organs	Papillary thyroid carcinoma	391	351	100.0	0.0	0.0	0	
	Follicular thyroid carcinoma	154	128	100.0	0.0	0.0	0	
	Medullary thyroid carcinoma	111	91	100.0	0.0	0.0	0	
	Anaplastic thyroid carcinoma	45	41	90.2	9.8	0.0	0	
	Adrenal cortical adenoma	50	35	100.0	0.0	0.0	0	
	Adrenal cortical carcinoma	26	25	100.0	0.0	0.0	0	
	Phaeochromocytoma	50	50	100.0	0.0	0.0	0	
	Appendix, neuroendocrine tumor (NET)	22	11	100.0	0.0	0.0	0	
	Colorectal, neuroendocrine tumor (NET)	12	9	100.0	0.0	0.0	0	
	lleum, neuroendocrine tumor (NET)	49 10	44	100.0	0.0	0.0	0	
	Lung, neuroendocrine tumor (NET) Pancreas, neuroendocrine tumor (NET)	19 97	17 91	100.0 98.9	0.0 0.0	0.0 0.0	0 1	
	Colorectal, neuroendocrine carcinoma (NEC)	12	9 i 8	96.9 87.5	0.0	0.0	12	
	Gallbladder, neuroendocrine carcinoma (NEC)	4	4	75.0	25.0	0.0	0	
	Pancreas, neuroendocrine carcinoma (NEC)	14	14	100.0	0.0	0.0	0	
Tumors of	Hodgkin Lymphoma	103	92	80.4	18.5	1.1	0	
naemotopoetic and	Small lymphocytic lymphoma, B-cell type (B-SLL/B-CLL)	50	52 50	100.0	0.0	0.0	C	
lymphoid tissues	Diffuse large B cell lymphoma (DLBCL)	113	112	100.0	0.0	0.0	C	
•	Follicular lymphoma	88	88	100.0	0.0	0.0	0	
	T-cell Non Hodgkin lymphoma	25	23	78.3	17.4	0.0	4	
	Mantle cell lymphoma	18	18	100.0	0.0	0.0	C	
	Marginal zone lymphoma	16	16	100.0	0.0	0.0	C	
	Diffuse large B-cell lymphoma (DLBCL) in the testis	16	16	100.0	0.0	0.0	C	
	Burkitt lymphoma	5	5	100.0	0.0	0.0	C	
Tumors of soft	Tenosynovial giant cell tumor	45	40	100.0	0.0	0.0	C	
tissue and bone	Granular cell tumor	53	39	100.0	0.0	0.0	(
	Leiomyoma	50	48	100.0	0.0	0.0	C	
	Leiomyosarcoma	87	84	98.8	1.2	0.0	C	
	Liposarcoma	132	106	98.1	1.9	0.0	C	
	Malignant peripheral nerve sheath tumor (MPNST)	13	12	100.0	0.0	0.0	C	
	Myofibrosarcoma	26	26	96.2	3.8	0.0	(
	Angiosarcoma	73	58	100.0	0.0	0.0	C	
	Angiomyolipoma	91	83	100.0	0.0	0.0	C	
	Dermatofibrosarcoma protuberans	21	15	100.0	0.0	0.0	C	
	Ganglioneuroma	14	12	100.0	0.0	0.0	C	
	Kaposi sarcoma	8	3	100.0	0.0	0.0	C	
	Neurofibroma	117	81	100.0	0.0	0.0	(
	Sarcoma, not otherwise specified (NOS)	74	66	98.5	1.5	0.0	C	
	Paraganglioma	41	30	56.7	33.3	10.0	(
	Ewing sarcoma	23	16	100.0	0.0	0.0	(
	Rhabdomyosarcoma	6	6	100.0	0.0	0.0	(
	Schwannoma	121	91	100.0	0.0	0.0	C	
	Synovial sarcoma	12	11	90.9	9.1	0.0	(
	Osteosarcoma	43	30	100.0	0.0	0.0	(
	Chondrosarcoma	38	23	100.0	0.0	0.0	C	

w or absent GATA3 immunostaining was linked to verse tumor features in breast cancers of no ecial type and in urothelial neoplams.

			GATA3 immunostaining result				
		n	neg. (%)	weak (%)	mod. (%)	strong (%)	Р
Primary Tumor	pTa G2 low	147	0.0	0.0	0.7	99.3	0.0109
•	pTa G2 high	117	0.0	0.0	1.7	98.3	
	pTa G3	161	3.7	0.6	3.1	92.5	
	pT2	132	25.8	13.6	19.7	40.9	0.7605
	pT3	222	30.6	11.7	16.7	41.0	
	pT4	107	30.8	13.1	12.1	43.9	
Regional Lymph	pN0	275	30.2	14.2	18.9	36.7	0.1303
Nodes	pN+	170	25.7	10.5	15.8	48.0	
p63 status	negative	25	28.0	0.0	28.0	44.0	0.0644
	positive	149	25.5	12.8	16.8	45.0	