



Supplementary Information for

Conserved serum protein biomarkers associated with growing early colorectal adenomas

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Supplementary Table S1. An overview of CTC patient data.

CTC Case #	Sex	Post-polypectomy blood draw*	Path Report Segment	Path Report Diagnosis	Length of Time On Study (Years)	Linear Size at final CTC (mm)	First/Final Volume measurement (mm ³)	Percent Growth By Volume	Growth classification based on volume (+/-30% Cutoff)	Overall Patient Growth Classification	Risk classification (based on standard-of-care criteria)
1	M		Rectosigmoid	Tubular adenoma	5.10	9.3	87/88	1.1	Static	Static	Low-Risk
2	M		Sigmoid	Tubular adenoma	5.10	8.2	28/83	196.4	Growing	Growing	Low-Risk
3	F		Transverse	Tubular adenoma, lymphoid follicle	5.33	6.7	36/45	25.0	Static	Static	Low-Risk
5	F		Ascending	Hyperplastic polyp	5.33	20.8	38/227	497.4	Growing	Growing	High-risk
			Rectum	Tubular adenoma	N/A	N/A	N/A		Unknown		
6	M		Rectum	Tubular adenoma	5.42	6.2	8/60	650.0	Growing	Growing	High-risk
			Sigmoid Colon Polyp	Hyperplastic polyp	N/A	N/A	N/A		Unknown		
7	M		Cecum	Tubulovillous Adenoma	5.61	13.7	33/900	2627.3	Growing	Growing	High-risk
8	F	No	Distal Sigmoid	Inflammatory Polyp	2.01	11.0	300/393	31.0	Growing	Growing	High-risk
			Proximal Sigmoid	Tubular adenoma	N/A	N/A	N/A		Unknown		
			Mid Sigmoid	Tubular adenoma	N/A	N/A	N/A		Unknown		
9	F		Ascending	Tubular adenoma	5.02	7.7	12/19	58.3	Growing	Growing	Low-Risk
10	F		Ascending	Inflammatory	7.18	8.7	--/266		Unknown	Unknown	High-risk
11	M	No	Hepatic flexure	Tubular adenoma	N/A	N/A	N/A		Unknown	Unknown	Low-Risk
			Sigmoid colon	Tubular adenoma	N/A	N/A	N/A		Unknown		
12	F		Cecum	Tubular adenoma	N/A	N/A	N/A		Unknown	Unknown	High-risk
			Cecum	Tubular adenoma	1.05	5.6	42/26	-38.1	Regressing		
13	M	No	Ascending	Sessile Serrated Adenoma	2.02	6.6	169/91	-46.2	Regressing	Regressing	High-risk
			Ascending	Sessile Serrated Adenoma	2.02	6.2	97/58	-40.2	Regressing		
15	F		Transverse	Tubular adenoma	4.84	4.0	13/7	-46.2	Regressing	Growing	High-risk
			Ascending	Tubular adenoma	4.84	5.0	60/13	-78.3	Regressing		
			Missing in path report	Tubular adenoma	4.84	7.7	60/91	51.7	Growing		
16	M		Rectosigmoid	Tubular adenoma	5.01	6.0	8/53	562.5	Growing	Growing	High-risk
			Transverse	Tubular adenoma	N/A	N/A	N/A		Unknown		
17	M		Descending	Tubular adenoma	N/A	N/A	N/A		Unknown	Growing	Low-Risk
			Sigmoid	Hyperplastic polyp	5.05	6.4	12/41	241.7	Growing		
			Ascending	Tubular adenoma	5.05	5.4	--/28		Unknown		
18	M		Hepatic flexure	Tubular adenoma	3.18	9.1	174/257	47.7	Growing	Growing	Low-Risk
			Rectum	Tubular adenoma and hyperplastic polyp	N/A	N/A	N/A		Unknown		
19	M		Sigmoid	Tubular adenoma	7.47	5.6	8/40	400.0	Growing	Growing	High-risk
			Sigmoid	Tubular adenoma	7.47	5.5	36/41	13.9	Static		
			Descending	Tubular adenoma	N/A	N/A	N/A		Unknown		
20	M		Sigmoid	Tubulovillous Adenoma	4.12	9.2	89/100	12.4	Static	Static	High-risk
21	M		Descending	Tubulovillous Adenoma	6.00	10.2	178/113	-36.5	Regressing	Unknown	High-risk
			Cecum/Ascending	Tubular adenoma	N/A	N/A	N/A		Unknown		
22	M		Cecum	Tubular adenoma	3.08	6.0	76/61	-19.7	Static	Unknown	High-risk
			Illeocecal valve	Tubular adenoma	3.08	6.6	59/65	10.2	Static		
			Ascending	Tubular adenoma	N/A	N/A	N/A		Unknown		
23	F		Sigmoid	Tubulovillous Adenoma	4.20	7.0	104/161	54.8	Growing	Growing	High-risk
			Ascending	Lymphoid Aggregate	N/A	N/A	N/A		Unknown		
			Rectum	Hyperplastic polyp	N/A	N/A	N/A		Unknown		
24	M		Rectum	Tubulovillous Adenoma	3.25	11.4	134/211	57.5	Growing	Growing	High-risk
			Rectosigmoid	Tubular adenoma	3.62	10.8	43/219	409.3	Growing		
25	M		Splenic Flexure	Tubular adenoma	N/A	N/A	N/A		Unknown	Growing	High-risk
			Descending	Hyperplastic polyp	N/A	N/A	N/A		Unknown		
			Ascending	Tubular adenoma	N/A	N/A	N/A		Unknown		
			Transverse	Tubular adenoma	N/A	N/A	N/A		Unknown		
26	M		Rectum	Hyperplastic polyp	3.11	6.1	28/31	10.7	Static	Unknown	Low-Risk
			Sigmoid	Hyperplastic polyp	N/A	N/A	N/A		Unknown		

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28	F		Sigmoid	Tubular adenoma and hyperplastic polyp	3.40	6.1	16/25	56.3	Growing	Growing	High-risk
			Rectum	Tubular adenoma	3.40	9.0	56/94	67.9	Growing		
			Ascending	Tubular adenoma	N/A	N/A	N/A		Unknown		
			Transverse	Hyperplastic polyp	N/A	N/A	N/A		Unknown		
29	F		Descending	Hyperplastic polyp	N/A	N/A	N/A		Unknown	Unknown	High-risk
			Cecum	Sessile Serrated Adenoma	5.02	7.8	40/35	-12.5	Static		
30	F	No	Transverse	Sessile Serrated Adenoma	N/A	N/A	N/A		Unknown	Growing	High-risk
			Cecum	Tubulovillous Adenoma	5.05	14.3	54/238	340.7	Growing		
32	M		Cecum	Tubular adenoma	5.05	9.9	76/86	13.2	Static	Growing	Low-Risk
			Ascending	Tubular adenoma	N/A	N/A	N/A		Unknown		
33	F		Descending	Tubular adenoma	5.27	10.4	161/321	99.4	Growing	Growing	High-risk
			Ascending	Sessile Serrated Adenoma	7.98	6.2	11/17	54.5	Growing		
34	M	No	Transverse	Tubular adenoma	7.98	7.0	--/21		Unknown	Growing	High-risk
			Transverse	Tubular adenoma	10.69	9.3	30/70	133.3	Growing		
35	M	No	Ascending	Tubular adenoma	N/A	N/A	N/A		Unknown	Unknown	High-risk
			Ascending	Tubular adenoma	3.51	8.0	45/46	2.2	Static		
35	M	No	Splenic flexure	Tubular adenoma	N/A	N/A	N/A		Unknown	Unknown	High-risk

*Post-polypectomy blood draw was obtained unless otherwise indicated.

Supplementary Table S2. Target protein biomarker sequences, reference standards, and monitored charge states and ions for LC/MS analysis.

Protein Name	Protein Symbol	Endogenous Peptide Sequence	Peptide Reference Standard Sequence*	Dominant Charge State	Peptide Ions Monitored (Qtrap 5500)	Peptide Ion Quantified
CD44 antigen	CD44	YGFIEGHVVIPR	YGFIEGHV V I*P*R	3	y4, y5, y6	y4
Complement Factor I	CFI	VFSLQWGEVK	VFSLQWGE V *K	2	y5, y6, y7, y8	y5
Leucine-Rich alpha-2-glycoprotein	Lrg1	VAAGAFQGLR	VAAGAFQGL* R (13C labeled only)	2	y5, y7, y8, y9	y8
Epidermal Growth Factor Receptor	EGFR	IPLLENLQIIR	IPLLENLQI I *R (13C labeled only)	2	y5, y6, y7, y8	y7
Inter-alpha-trypsin inhibitor heavy chain H3	Itih3	EVSFDVELPK	EVSFDVEL* P K (13C labeled only)	2	y5, y6, y7, y8	y5
Coagulation factor V	F5	NFFNPPIISR	NFFNPPII* S R (13C labeled only)	2	y6, y7, y8, b8	y6
Hemopexin	Hpx	LWWLDLK	LWWLDL* K (13C labeled only)	2	y4, y5, y6, b5	y5
Vitamin D-binding protein	Gc	VLEPTLK	VLEPTL* K (13C labeled only)	2	y4, y5, y6	y4
Vitronectin	VTN	FEDGVLDPDYPR	FEDGVLDPDY P *R	2	y5, y6, y7, y8	y5
Inter-alpha-trypsin inhibitor, Heavy chain 4	ITIH4	FAHTVVTSR	FAHTV V T*SR	3	y3, y4, b3, b4	y3
Serum Amyloid P	APCS	GYVLIKPLVWV	GYVLIK P L*VWV (13C labeled only)	2	y6, y7, y8, b9	b9
Fetuin B	FetuB	IFFESVYGQCK	IFFESVYGQ C *K	2	y6, y7, y8, y9	y9
C-reactive protein	Crp	ESDTSYVSLK	ESDTSYVSL* K (13C labeled only)	2	y5, y6, y8	y6
Sulfhydryl Oxidase 1	QSOX1	LAGAPSEDPQFPK	LAGAPSEDPQF P *K	2	y5, y7, y9, b4	y9
Peptidase inhibitor 16	PI16	WDEELAAFAK	WDEELAA F *K	2	y6, y8, y9	y8
Cadherin-2 (N-Cadherin)	Cdh2	GPFQELVR	GPFQEL* V R (13C Labeled Only)	2	y6, y7, b3	y6
Dipeptidyl peptidase 4	DPP4	WEYYDSVYTER	WEYYDSV Y *TER	2	y7, y8, y9, b5	y9
extracellular superoxide dismutase [Cu-Zn]	Sod3	VTGVVLFRR	VTGVV L *FR (13C Labeled Only)	2	y4, y5, y6, y7	y6
Thrombospondin-4	Thbs4	DVDIDSYPDEELPCSAR	DVDIDSYPDEEL P CSA*R	2	y5, y9, y10, b7	y10

Bolded* indicates the amino acid labeled with ¹³C¹⁵N unless otherwise indicated

Supplementary Table S3. An overview of patient data from optical colonoscopy.

Sample Number	Sex	Number of Polyps Identified	Pathology Diagnosis	Adenoma Risk classification (based on pathology)
31227	F	1	Large Sessile Serrated Adenoma	High-Risk
31273	F	4	Hyperplastic polyp and family history	High-Risk
23051	F	7	Hyperplastic polyps	High-Risk
31633	F	1	Large sessile serrated adenoma	High-Risk
30653	F	4	Multiple sessile serrated adenomas	High-Risk
31527	F	9	Multiple tubular adenomas and hyperplastic polyps	High-Risk
21344	F	3	non-neoplastic colonic mucosa, multiple biopsies	High-Risk
22910	F	1	Tubular adenoma	High-Risk
31489	F	2	Large tubular adenoma and sessile serrated adenoma	High-Risk
22911	F	2	Tubular adenoma and benign colonic mucosa	High-Risk
31532	F	2	Tubular adenoma and large hyperplastic polyp	High-Risk
23252	F	2	Tubular adenomas	High-Risk
21489	F	1	Tubulovillous adenoma	High-Risk
31472	M	1	Hyperplastic polyp and family history	High-Risk
31530	M	4	Multiple sessile serrated adenomas	High-Risk
30771	M	6	Multiple tubular adenomas	High-Risk
23061	M	3	Normal mucosa/lymphoid aggregates, tubular adenoma	High-Risk
22797	M	7	Sessile serrated polyp/adenoma and hyperplastic polyps	High-Risk
30651	M	2	Large tubular adenoma and hyperplastic polyp	High-Risk
31611	M	1	Tubular adenoma and family history	High-Risk
21528	M	2	Tubular adenoma and sessile serrated polyp	High-Risk
21756	M	2	Tubular adenoma, and tubulovillous adenoma	High-Risk
22887	M	9	Tubular adenomas and hyperplastic polyps	High-Risk
22798	M	5	Tubular adenomas and a large tubulovillous adenoma	High-Risk
22928	F	2	Benign colonic mucosa, multiple biopsies	Low-Risk
31634	F	0	Gastric biopsies, colonoscopy normal	Low-Risk
21216	F	1	Hyperplastic polyp	Low-Risk
30497	F	1	Hyperplastic polyp	Low-Risk
22927	F	1	Hyperplastic polyp and benign colonic mucosa	Low-Risk
31488	F	2	Hyperplastic polyps	Low-Risk
31471	F	2	Sessile serrated adenoma/polyp	Low-Risk
21214	F	1	Tubular adenoma	Low-Risk
21527	F	1	Tubular adenoma	Low-Risk
21837	F	1	Tubular adenoma	Low-Risk
22872	F	1	Tubular adenoma	Low-Risk
30629	F	1	Tubular Adenoma	Low-Risk
31612	F	1	Tubular adenoma	Low-Risk
31947	F	1	Tubular Adenoma	Low-Risk
22891	F	3	Tubular adenoma and hyperplastic polyp	Low-Risk
22892	F	3	Tubular adenoma and hyperplastic polyp	Low-Risk
23060	F	2	Tubular adenoma and normal mucosa	Low-Risk
21478	M	1	Hyperplastic polyp	Low-Risk
21968	M	2	Hyperplastic polyps	Low-Risk

Sample Number	Sex	Number of Polyps Identified	Pathology Diagnosis	Adenoma Risk classification (based on pathology)
22848	M	0	Ischemic colitis	Low-Risk
23250	M	1	Lymphoid nodule, sessile serrated adenoma	Low-Risk
23251	M	1	Mucosal lymphoid nodule/normal mucosa	Low-Risk
23254	M	1	Mucosal lymphoid nodule/normal mucosa	Low-Risk
21474	M	3	Nondysplastic mucosa and tubular adenoma	Low-Risk
23248	M	1	Normal mucosa	Low-Risk
22800	M	1	Sessile serrated adenoma/polyp	Low-Risk
21154	M	1	Tubular adenoma	Low-Risk
21529	M	1	Tubular adenoma	Low-Risk
21836	M	2	Tubular adenoma	Low-Risk
22869	M	1	Tubular adenoma	Low-Risk
22929	M	1	Tubular Adenoma	Low-Risk
22989	M	1	Tubular Adenoma	Low-Risk
23042	M	1	Tubular Adenoma	Low-Risk
21488	M	2	Tubular adenoma, and hyperplastic polyp	Low-Risk
23039	M	1	Tubular Adenoma, Colectomy	Low-Risk
23247	M	2	Tubular adenoma/Hyperplastic polyp	Low-Risk
31167	M	2	Tubular Adenomas	Low-Risk
30628	M	2	Tubular Adenomas	Low-Risk
22997	M	3	Tubular adenomas/Normal mucosal polyp	Low-Risk
21685	F	N/A	Screening Normal	N/A
21755	F	N/A	Screening Normal	N/A
21530	F	N/A	Screening Normal	N/A
22888	F	N/A	Screening Normal	N/A
22909	F	N/A	Screening Normal	N/A
21958	F	N/A	Screening Normal	N/A
22987	F	N/A	Screening Normal	N/A
22988	F	N/A	Screening Normal	N/A
23031	F	N/A	Screening Normal	N/A
30431	F	N/A	Screening Normal	N/A
30967	F	N/A	Screening Normal	N/A
31090	F	N/A	Screening Normal	N/A
31248	F	N/A	Screening Normal	N/A
21155	M	N/A	Screening Normal	N/A
21684	M	N/A	Screening Normal	N/A
22847	M	N/A	Screening Normal	N/A
22849	M	N/A	Screening Normal	N/A
22996	M	N/A	Screening Normal	N/A
23059	M	N/A	Screening Normal	N/A
23032	M	N/A	Screening Normal	N/A
30517	M	N/A	Screening Normal	N/A
23076	M	N/A	Screening Normal	N/A
23253	M	N/A	Screening Normal	N/A
31571	M	N/A	Screening Normal	N/A
30432	M	N/A	Screening Normal	N/A

Sample Number	Sex	Number of Polyps Identified	Pathology Diagnosis	Adenoma Risk classification (based on pathology)
31130	M	N/A	Screening Normal	N/A
31528	M	N/A	Screening Normal	N/A

Supplementary Tables S4a-c. Quantitation by targeted mass spectrometry of the levels of the 19 candidate serum proteins in patients from the CTC and OC cohorts.

Supplementary Table S4a. Panel 4a presents the median ratios of the test samples to the labeled peptide standard for each protein of interest.

Median Ratio-to-Reference Standard

Protein	Screening Normal Relative Ratio-to-Standard	Unknown Growth Relative Ratio-to-Standard	Growing Relative Ratio-to-Standard	Growing High-Risk Relative Ratio-to-Standard
QSOX1	0.211	0.218	0.222	0.213
F5	0.859	0.859	1.184	1.183
ITIH4	1.781	1.664	2.012	1.971
CRP	0.317	0.473	0.885	0.894
LRG1	2.992	3.006	3.375	3.473
DPP4	0.080	0.080	0.074	0.076
EGFR	0.052	0.052	0.054	0.053
SOD3	0.146	0.154	0.169	0.167
CDH2	0.022	0.023	0.024	0.021
HPX	7.862	6.653	8.028	6.399
ITIH3	1.564	1.529	1.722	1.779
APCS	6.863	6.674	6.713	6.855
FETUB	4.618	4.680	4.750	4.661
GC (VitD)	1.401	1.376	1.435	1.401
CD44	0.713	0.694	0.722	0.708
CFI	4.360	4.217	4.672	5.271
PI16	0.473	0.476	0.469	0.434
THBS4	0.106	0.121	0.124	0.124
VTN	4.182	4.005	4.676	4.648

Supplementary Table S4b. Panel 4b presents the ratios that compare these medians between the sets of patients whose adenomas have been classified as Growing, Unknown Growth (likely non-growing), or (adenoma-free) Screening Normal. Significant differences at $p < 0.05$ are shown in red.

Comparison group ratio of ratios

Protein	Unknown Growth vs. Screening Normal	Growing vs. Screening Normal	Growing vs. Unknown Growth	Growing High-Risk vs. Screening Normal
QSOX1	1.035	1.054	1.018	1.013
F5	0.999	1.378	1.379	1.377
ITIH4	0.934	1.130	1.209	1.107
CRP	1.493	2.791	1.869	2.822
LRG1	1.005	1.128	1.123	1.161
DPP4	1.004	0.925	0.922	0.956
EGFR	1.003	1.038	1.035	1.012
SOD3	1.055	1.160	1.100	1.145
CDH2	1.047	1.059	1.012	0.940
HPX	0.846	1.021	1.207	0.814
ITIH3	0.978	1.101	1.126	1.137
APCS	0.972	0.978	1.006	0.999
FETUB	1.013	1.029	1.015	1.009
GC (VitD)	0.982	1.024	1.043	1.000
CD44	0.973	1.012	1.041	0.992
CFI	0.967	1.072	1.108	1.209
PI16	1.006	0.991	0.985	0.917
THBS4	1.147	1.171	1.021	1.175
VTN	0.957	1.118	1.168	1.111

Supplementary Table S4c. Panel 4c presents the non-parametric p-values for tests of difference between two specified groups of patients. Significant differences at $p < 0.05$ are shown in red.

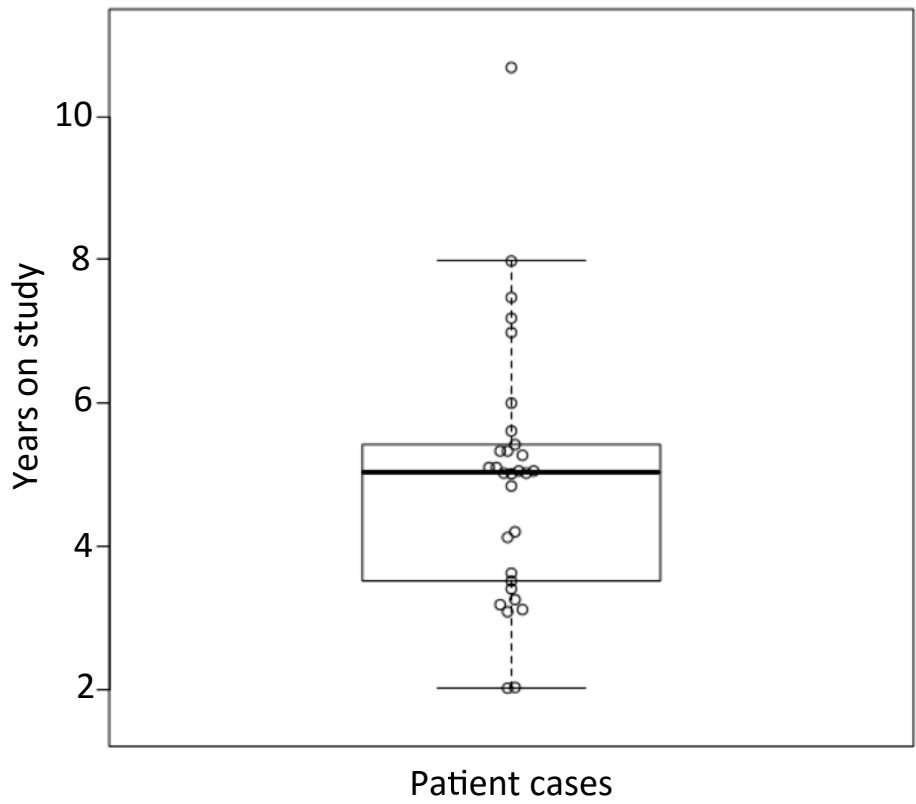
Mann-Whitney p-values for comparison groups

Protein	Unknown Growth vs. Screening Normal	Growing vs. Screening Normal	Growing vs. Unknown Growth	Growing High-Risk vs. Screening Normal
QSOX1	0.2543	0.0312	0.2554	0.1757
F5	0.9203	0.0005	0.0001	0.0029
ITIH4	0.1141	0.1548	0.0043	0.2938
CRP	0.1936	0.0045	0.0271	0.0017
LRG1	0.6527	0.0304	0.0331	0.0671
DPP4	0.5419	0.1984	0.4607	0.4088
EGFR	0.9761	0.9176	0.7962	0.8985
SOD3	0.5029	0.1978	0.3944	0.1847
CDH2	0.9840	0.4520	0.5840	0.9459
HPX	0.0703	0.3081	0.8360	0.1024
ITIH3	0.6892	0.6269	0.2042	0.9459
APCS	0.4533	0.8772	0.9053	0.9028
FETUB	0.5419	0.3297	0.8930	0.5408
GC (VitD)	0.4777	0.5071	0.3944	0.8175
CD44	0.4777	0.7740	0.4110	0.9028
CFI	0.4354	0.5770	0.2324	0.3183
PI16	0.3628	0.3081	0.3550	0.3334
THBS4	0.4777	0.3757	0.8829	0.3431
VTN	1.0000	0.0415	0.0859	0.1084

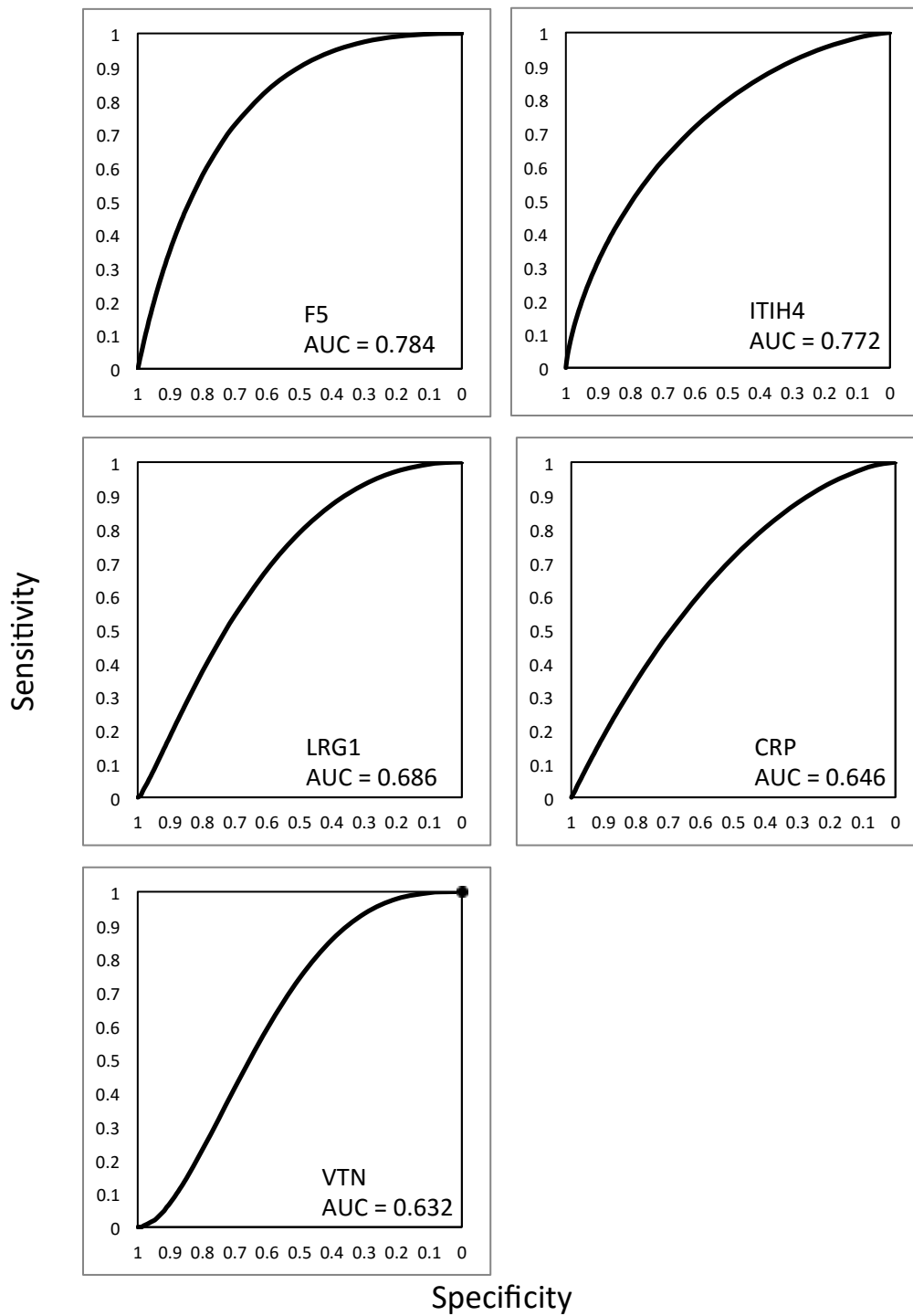
Supplementary Table S5

Logistic regression Analysis (Single variable) for Volumetric Growth vs. Unknown Growth

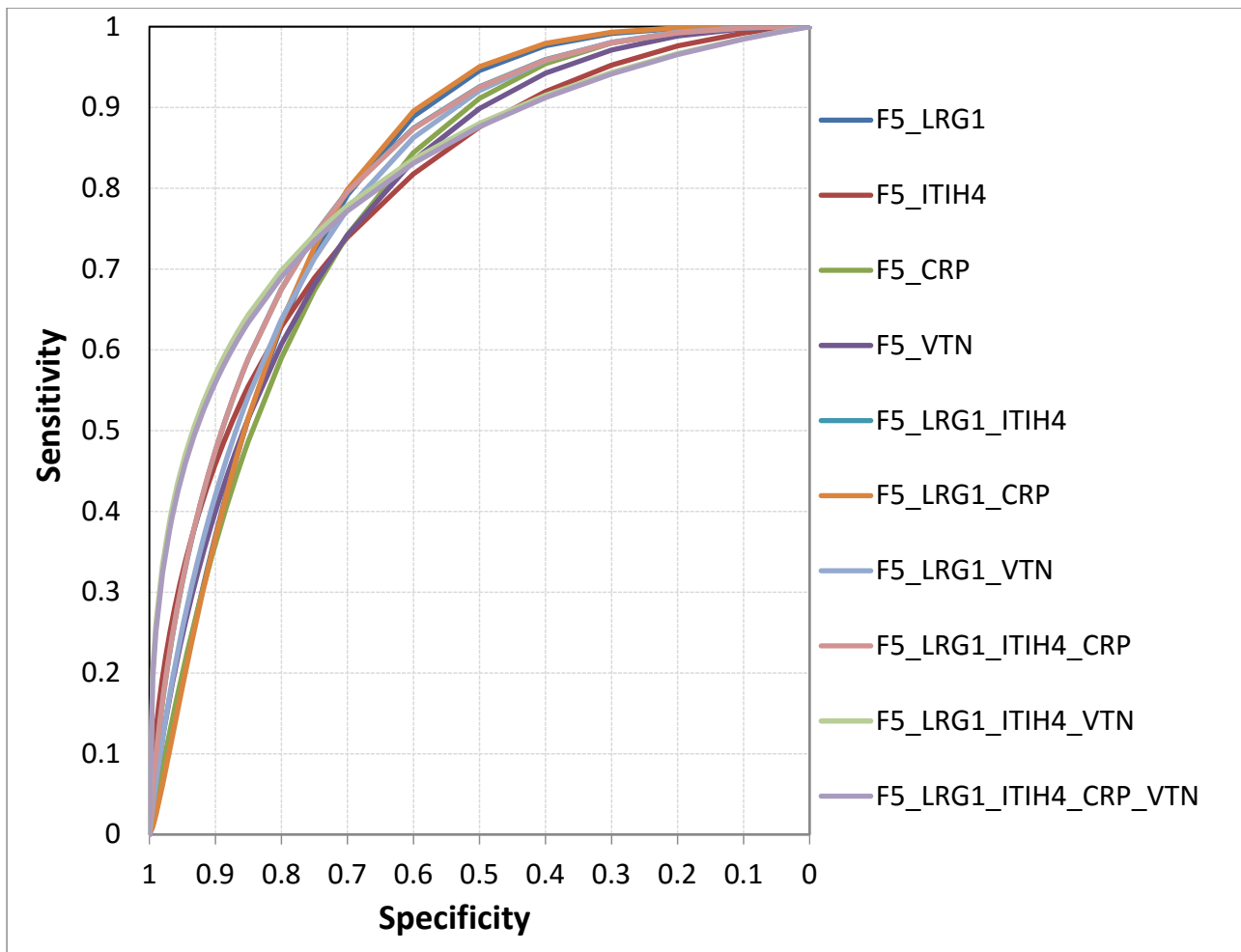
Protein	Chi Sq. Value	Chi P-value	CV	Std. Error	p-value	Odds Ratio	CI Low	CI high	AUC
F5	15.397	0.000	3.963	1.122	0.0004	52.608	5.837	474.157	0.784
ITIH4	76.000	0.002	2.099	0.746	0.0049	8.161	1.891	35.221	0.722
LRG1	4.949	0.026	0.630	0.290	0.0299	1.877	1.063	3.315	0.686
CRP	0.660	0.416	0.194	0.232	0.4032	1.214	0.770	1.915	0.646
VTN	2.472	0.116	0.321	0.210	0.1268	1.379	0.913	2.082	0.632
QSOX1	1.005	0.316	4.641	4.599	0.3128	103.680	0.013	3.674	0.599
CFI	2.069	0.150	0.296	0.207	0.1514	1.345	0.897	2.016	0.594
ITIH3	1.159	0.282	0.376	0.347	0.2786	1.457	0.738	2.876	0.589
PI16	0.870	0.351	-1.157	1.392	0.4058	0.314	0.021	4.814	0.567
VITD	0.888	0.346	1.148	1.229	0.3502	3.151	0.284	35.008	0.562
CD44	1.206	0.272	1.449	1.320	0.272	4.261	0.321	56.587	0.559
APCS	1.966	0.161	0.097	0.069	0.1577	1.102	0.963	1.261	0.552
THBS4	0.183	0.669	2.813	6.521	0.6662	16.653	1.97E-05	0.598	0.537
DPP4	0.339	0.561	-3.562	6.917	0.6066	0.028	2.19E-05	8.958	0.533
EGFR	0.625	0.429	-14.663	23.708	0.5363	<0.00001	6.17E-05	1.734	0.529
CDH2	0.408	0.523	20.507	31.972	0.5213	3.74E+04	<0.00001	1.321	0.526
FETUB	0.125	0.724	0.063	0.178	0.7232	1.065	0.752	1.509	0.516
HPX	0.102	0.749	-0.0291	0.092	0.7511	0.971	0.812	1.162	0.512
SOD3	0.272	0.602	-0.8764	1.889	0.6427	0.416	0.010	16.873	0.439



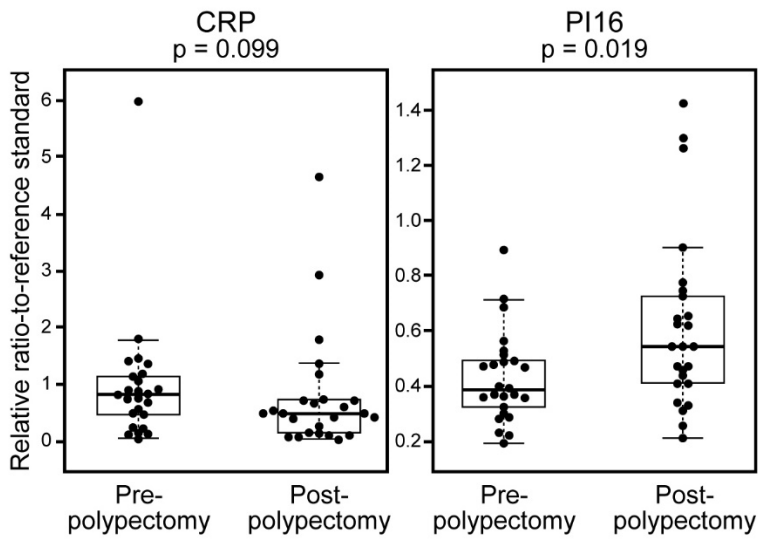
Supplementary Figure S1. Number of years each patient was monitored by CTC prior to polypectomy. Each circle represents one patient. The median number of years on study (thick black line) was 5 years.



Supplementary Figure S2. Individual protein ROC curves for growing versus unknown growth for top performing proteins. ROC curves were computed by Method 5 in the JROC fit calculation (Eng, J. ROC analysis: web-based calculator for ROC curves. 2017 Cited July 2017; Available from: <http://www.jrocfite.org>).



Supplementary Figure S3. Overlays of the ROC curves from multiple marker panel analyses. The ROC curves shown in Supplementary Figure 2 dictate that each of these panels lie in the top echelon. The panel F5, ITIH4, LRG1 and VTN ranked in this top echelon. It was subjected to the validation test on the set of early adenomas in the Pirc rat model (Ivancic et al. *Cancer Prev Res* 2014; 7:1160-1169).



Supplementary Figure S4. Group analysis of adenoma association of serum CRP and PI16 levels. Scatterplots show the distribution of the relative levels of the biomarkers CRP and PI16 across the set of adenoma-bearing patients. The median of each non-parametric distribution is given by the black central line of the box-and-whisker plot.

Supplementary Figure S5. Seventeen serum biomarkers for which the paired sample analysis fails to show specificity for ambient marker level or for adenoma class. For the seventeen serum biomarkers other than CRP and PI16 (which are shown in Figure 5), the calculated ratios of biomarkers level are plotted against their corresponding input, expressed as the post-polypectomy level. Black-filled symbols represent high risk cases; white-filled symbols represent low-risk cases.

