GI03
06/27/2020
11:48am

Jason Liggett, Ph.D., EDP Biotech

EDP BIOTECH CORPORATION
Early Detection Products

ColoPlex
Fight Cancer. Detect Early.

Serum based multiplex protein assay for early detection of colorectal cancer and precancerous lesions in a FIT positive population

June 30th, 2020

Presented by
Jason L. Liggett, PhD
jasonliggett@edpbiotech.com

NIH NATIONAL CANCER INSTITUTE
Early Detection Research Network

35th Steering Committee meeting

Acknowledgments

Department of Surgical Gastroenterology, Hvidovre Hospital, DK-2650 Hvidovre, Denmark

- Ib Jarle Christensen
- Linnea Ferm
- Hans Jørgen Nielsen

Fritsche Consulting Services, Houston, TX

- Herbert A. Fritsche

Department of Computer Science, Georgia Southern University, Statesboro, GA

- Hong Zhang

EDP Biotech Corporation, Knoxville, TN

- Selena Ledesma Alonso
- Jim Fetzer
- Brennan Hicks
- Anton Jansen
- Eric S. Mayer
- Olivia McGhee

Research Aims

- Validate a set of serological protein biomarkers, plexed together, which improve existing CRC screening programs:
  - Reduce endoscopy burden by orthogonal testing and/or reflexing FIT positives;
  - Provide convenient interval testing and/or alternative for FIT non-compliant population.

Biomarker Discovery: Wide Net

- Literature review
- Internal mass spec. data
- Known pathways
  - Angiogenesis
  - Metastasis
  - Cell Signaling
  - Cell cycle regulators
  - Immune evasion
  - Cytoskeletal proteins

Discovery - Patient Population

Hvidovre Hospital (Denmark) Endoscopy III

- 100 FIT+ Clean Colonoscopy
- 100 FIT+ CRC
  - 50 FIT+ CRC Stage I
  - 50 FIT+ CRC Stage II
- 199 FIT+ Adenomas
  - 99 FIT+ Low-Risk Adenomas
  - 100 FIT+ High-Risk Adenomas

European Polyp Guidelines:

High-risk adenomas (HRA): (re-colonoscopy within one year)
one lesion >= 20 mm or >=5 lesions or resected by piece-meal technique

Medium-risk adenomas (MRA): (re-colonoscopy within 3 years)
one lesion >= 10 mm but <20 mm or 3-4 lesions or presence of villous elements or high-grade neoplasia

Low-risk adenomas (LRA): (re-screening in two years)
lesion < 10 mm or <3 lesions or tubular histology or low-grade neoplasia

ColoPlex
Fight Cancer. Detect Early.

Luminex
xMAP® Technology

- Alpha-FetoProtein (AFP)
- Carcinoembryonic antigen (CEA)
- Cathepsin D
- Cluster Differentiation 44 (CD44)
- Ferritin
- Growth/differentiation factor 15 (GDF15)
- Hepsin
- Interleukin 8 (IL-8)
- Keratin 1 and Keratin 10 complex (KRT1/10)
- L1 Cell Adhesion Molecule (L1CAM)
- Melanoma Inhibitory Activity (MIA)
- Midkine
- Neuron Specific Enolase (NSE)
- Osteonectin (ON), Secreted Protein Acidic and Rich in Cysteine (SPARC)
- TNF-related WEAK inducer of apoptosis (TWEAK)
- YKL40

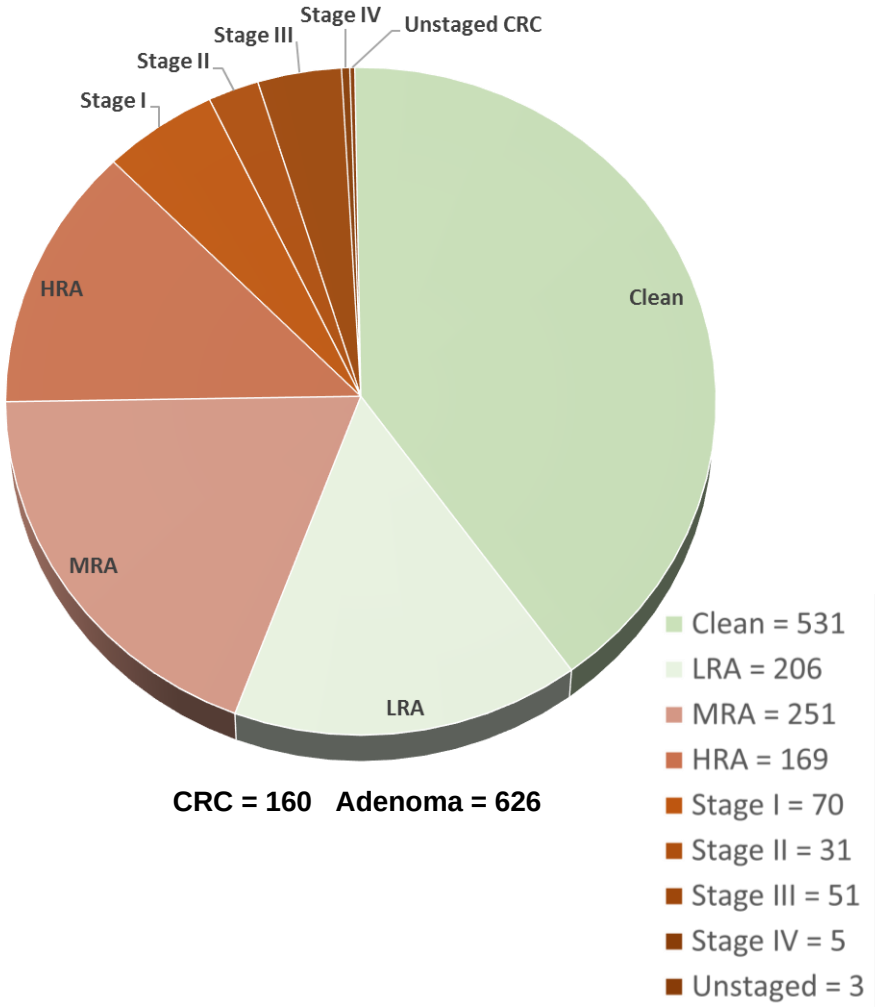
Validation: ENDO III Cohort

Hvidovre Hospital

Fig. 1

A

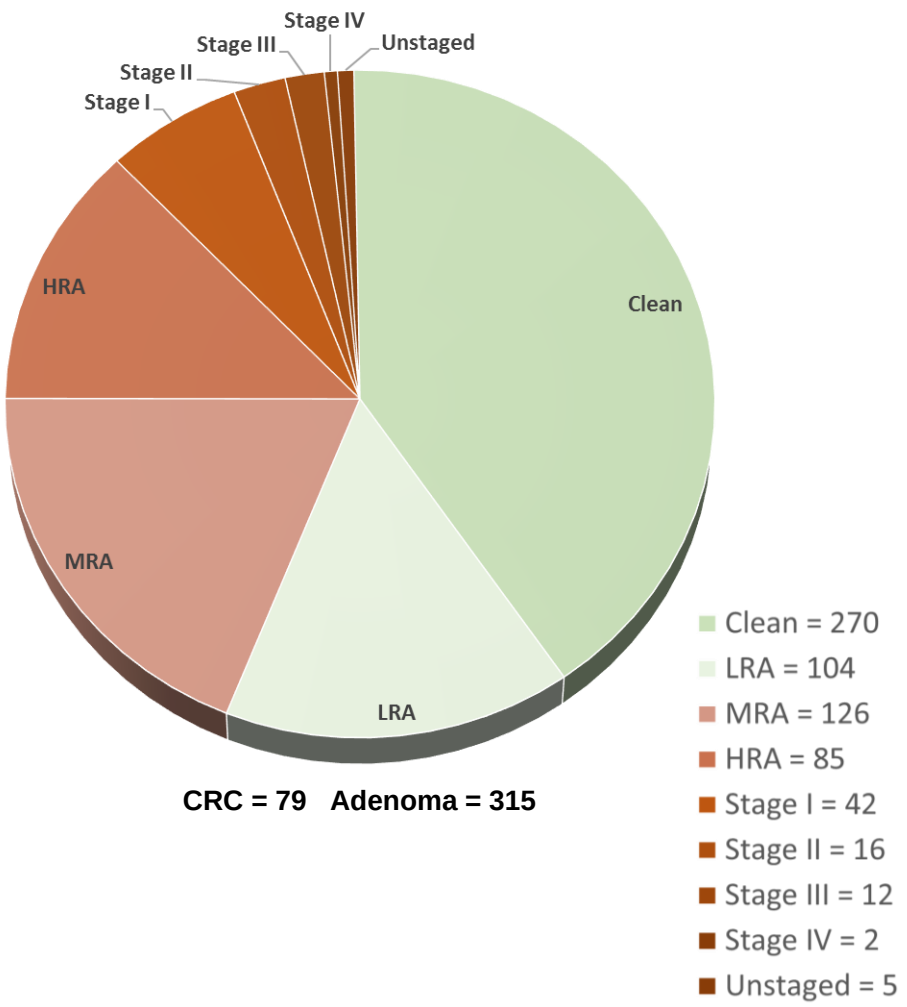
Training Set = 1317



CRC = 160 Adenoma = 626

B

Validation Set = 664



CRC = 79 Adenoma = 315

Univariate Analysis: CRC, HRA, MRA vs LRA, Clean

Table. 1

Outcome	Marker	Odds Ratio	OR Lower cl	OR Upper cl	P-value	AUC	Sensitivity at 30% specificity	Sensitivity at 70% specificity	Sensitivity at 80% specificity	Sensitivity at 90% specificity
CRC+HRA+MRA	AFP	1.01	0.93	1.11	0.7687	0.50	0.68	0.34	0.23	0.10
	CD44	1.01	0.80	1.27	0.9331	0.49	0.67	0.29	0.19	0.11
	CEA	1.14	1.03	1.26	0.0101	0.54	0.77	0.34	0.22	0.12
	Cathepsin-D	1.31	1.12	1.53	0.0006	0.56	0.80	0.36	0.22	0.11
	Ferritin	0.97	0.90	1.05	0.4911	0.51	0.71	0.32	0.23	0.13
	GDF-15	1.35	1.16	1.57	0.0001	0.58	0.84	0.38	0.23	0.09
	Hepsin	1.01	0.89	1.16	0.8301	0.49	0.70	0.28	0.17	0.09
	IL-8	1.26	1.12	1.42	0.0002	0.56	0.77	0.38	0.26	0.15
	Keratin1-19	0.99	0.92	1.05	0.6812	0.52	0.73	0.31	0.19	0.08
	L1CAM	0.95	0.82	1.1	0.5154	0.51	0.72	0.30	0.22	0.11
	MIA	1.09	0.82	1.46	0.5382	0.50	0.72	0.29	0.21	0.12
	MIDKINE	1.24	1.04	1.47	0.0147	0.54	0.75	0.38	0.22	0.11
	NSE	1.1	0.93	1.29	0.2544	0.53	0.75	0.33	0.23	0.11
	Osteonectin	1.24	1.01	1.51	0.0367	0.53	0.74	0.33	0.22	0.14
	TWEAK	1.01	0.80	1.26	0.9543	0.50	0.70	0.31	0.21	0.11
	YKL-40	1.11	1.01	1.22	0.0327	0.54	0.76	0.34	0.21	0.11
	MCP-1	1.1	0.91	1.33	0.3183	0.52	0.72	0.31	0.20	0.12
	OPG	1.25	0.96	1.62	0.0953	0.53	0.73	0.34	0.22	0.11

SVM Result: CRC, HRA, MRA vs LRA, Clean

(Support Vector Machines, supervised machine learning)

10 biomarkers + FIT concentration & Age

Ferritin, Keratin 1/10, L1CAM, IL-8, CEA, MIA, Hepsin, YKL-40, NSE, & GDF-15

Fig. 2 ROC curves

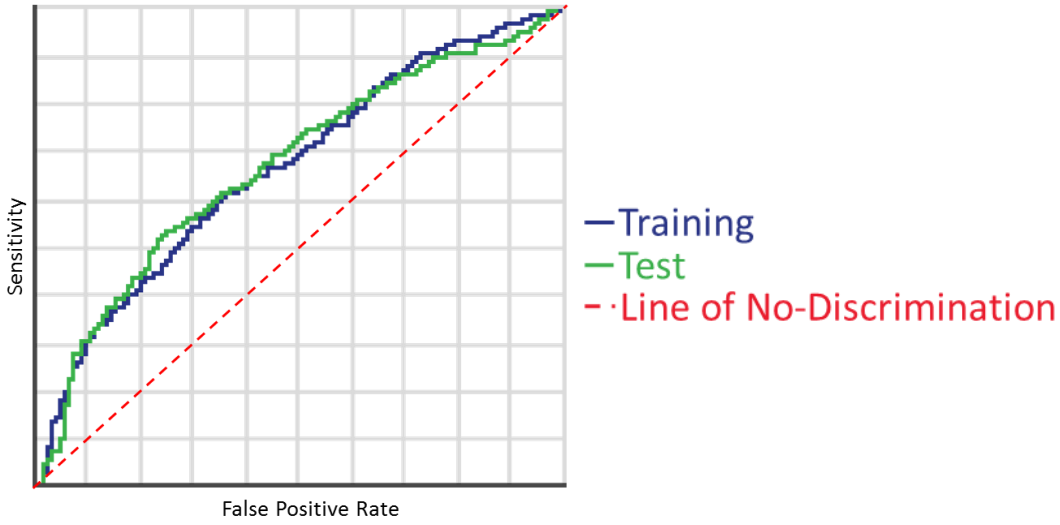
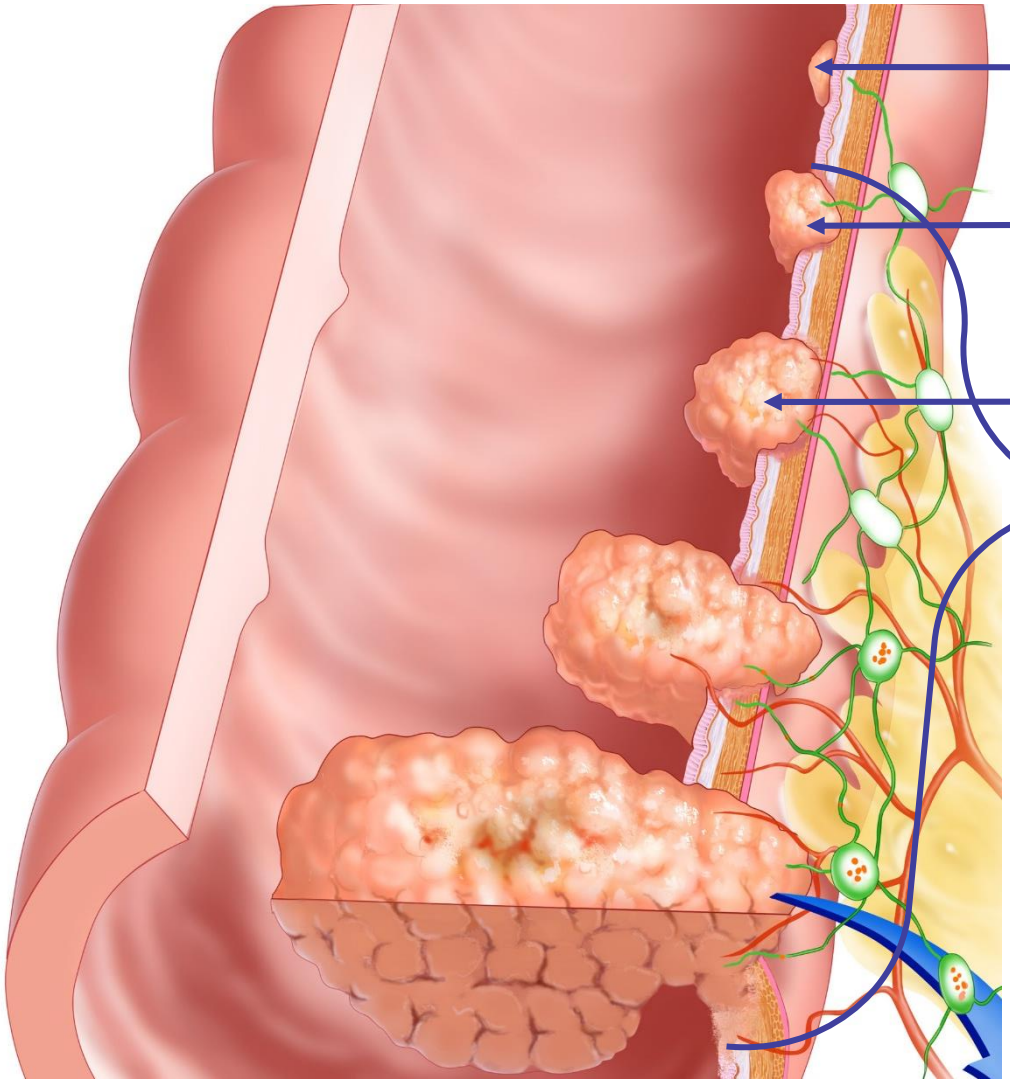


Table. 2

Dataset	Outcome	N	P-value	AUC	Sensitivity at 20% specificity	Sensitivity at 30% specificity	Sensitivity at 70% specificity	Sensitivity at 80% specificity	Sensitivity at 90% specificity
Training	CRC+HRA+MRA	1317	<0.0001	0.662	0.93	0.87	0.54	0.41	0.30
Validation	CRC+HRA+MRA	664	<0.0001	0.673	0.90	0.86	0.57	0.46	0.32

Early Detection: SVM 10 marker + FIT & age, validation



Pre-cancer sensitivity **89%**
(polyp > 10 mm)

Cancer Stage I sensitivity **90%**

Cancer Stage II sensitivity **100%**

Cancer (Stages I-IV)
sensitivity **94%**

Table. 3

A

CRC	Pos	Neg	TPR	
Unstaged	5	0	100%	94%
IV	4	0	100%	
III	11	1	92%	
II	16	0	100%	
I	38	4	90%	

B

Adenoma	Pos	Neg	TPR	
HRA	80	5	94%	89%
MRA	107	19	85%	

C

Low Risk	Pos	Neg	FPR	
LRA	81	23	78%	78%
Clean	212	58	79%	

Conclusions:

- Our research demonstrates the feasibility of blood-based protein biomarkers to:
  - Complement FIT in orthogonal/reflex modality to catch most true positives and reduce false positives.
  - Complement screening programs by offering a convenient blood test for patients who refuse or are non-compliant with guidelines.
- Additional studies in FIT non-compliant &/or negative population, and interval studies between colonoscopy, are needed to confirm these results.

EDP BIOTECH CORPORATION
Early Detection Products

5 minute Q&A

Chair/Co-Chair/NCI
feed Zoom Chat questions to presenter
and Track Time
NCI and Production Team
answer Chat questions not related to presentations
and use Slack