



BIOTECH SUPPORT GROUP
Sample Prep that Matters

CANCER PROTEOMICS APPLICATION REPORT

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Stroma Liquid Biopsy - Proteomic Profiles for Cancer Biomarkers

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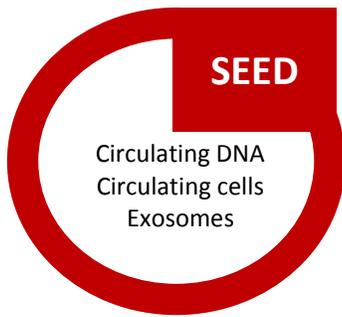
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Introduction and Objectives

While the landscape of cancer-associated DNA mutations has supported the initial concepts for liquid biopsy, it is now overwhelmingly apparent that throughout cancer progression, there are necessary adaptive microenvironments to support metastatic disease. We now present evidence that some of the essential interactions between stroma and proliferating cells can in part, be monitored through the protein response that tracks into the vascularized tumor and re-proportions the extracellular proteins (serum) found in the general blood circulation. These patent pending proteomic patterns can now be reported as a Stroma Liquid Biopsy[™].

What if there was a way to form an early indicator for cancer, possibly before clinical evidence, and with personalized tie-in to therapies? That opportunity starts with cancer's microenvironments – the SOIL !

Liquid Biopsy Genomic Evidence



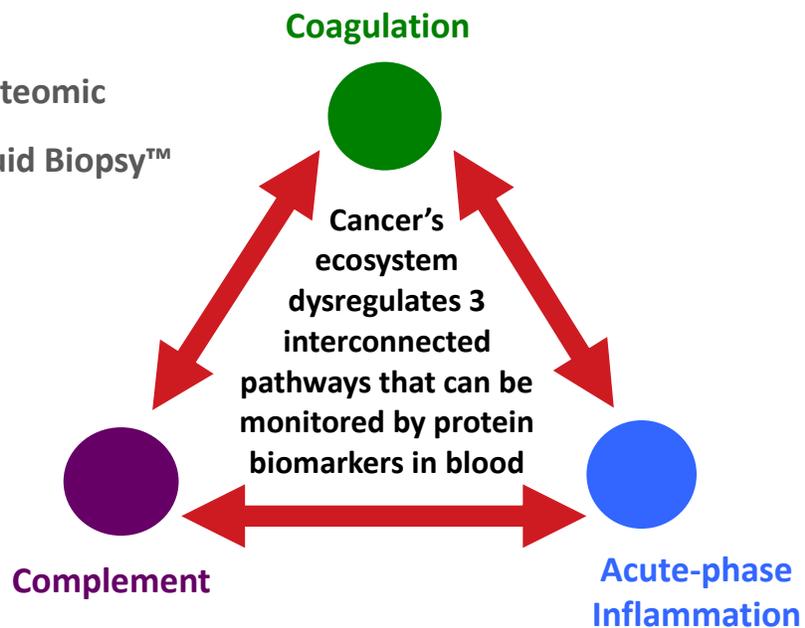
- Heterogeneous nature of cancer's DNA has confounded real progress in detection and treatment.
- Cooperative relationship between cancer cells and a repertoire of recruited, normal host cells referred to as the **stroma**^{1,2}
- All the SEED approaches, miss an essential element of cancer pathogenesis, the tumor-associated microenvironment.

Stroma Liquid Biopsy™ Proteomic Evidence



Interactions between stroma and proliferating cells, re-proportions biomarker proteins of moderate to high abundance found in the general blood circulation

● Demanding a proteomic approach, Stroma Liquid Biopsy™ offers that new view



Stroma Liquid Biopsy™ Profile of Serum Proteome Dysregulation in Cancer

Methods

LC-MS/MS provides an alternative assay approach to immunoassays, relying on the discriminating power of mass analyzers to observe specific peptides as surrogates for protein(s) and ion current intensities for quantitation. Most importantly, LC-MS/MS provides a singular platform for profiling multiple biomarkers in one analysis across a wide concentration range; in our case, serum concentrations typically spanning [ng-mg]/ml, with most in the µg/ml range. Discovery methods have been previously reported^{3,4}.

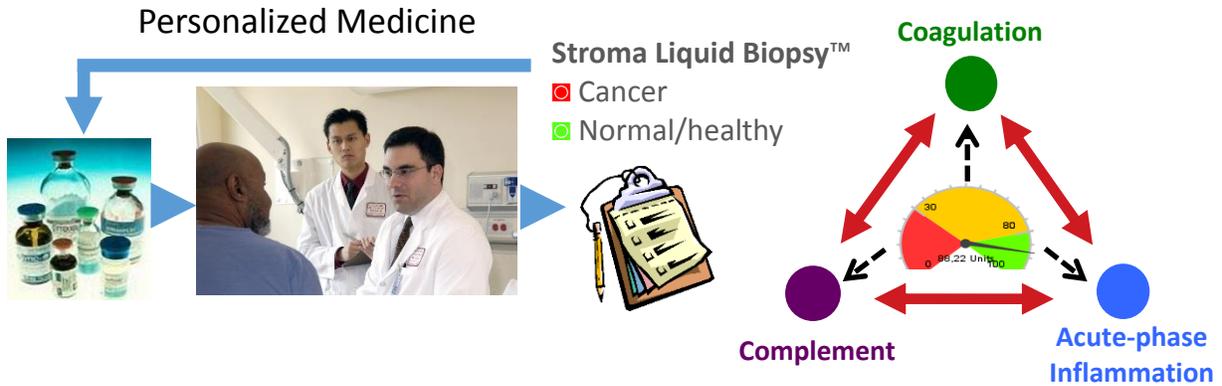
Protein Conc. Range > 5 log measurable in 1 LC-MS Analysis		Normal/Healthy Females, age 40-60				Cancer Females, age 40-60				
Systemic Pathway	Rakta Protein Code	N1	N2	N3	N4	Breast Stg 1	Lung Stg 2	N-Hod Lymph	Panc Stg 2b	Ova-ry
Coagulation	CA	Nd	0.3	0.4	Nd	0.8	3.2	4.0	1.0	2.5
Coagulation	CB	5	3	2	3	107	201	26	80	15
Coagulation	CC	Nd	Nd	Nd	Nd	39	87	11	22	11
Coagulation	CD	0.1	Nd	Nd	Nd	7	11	2	4	1
Coagulation	CE	1.0	1.4	0.9	1.5	0.6	0.5	0.3	0.2	0.2
Complement	TA	1.8	1.3	1.6	1.3	1.2	0.5	1.1	0.5	0.5
Complement	TB	3.1	1.2	1.5	2.6	0.8	3.2	0.6	0.8	0.2
Complement	TC	2.5	1.6	1.3	2.3	1.2	1.5	0.6	0.8	0.4
Acute-phase Inflammation	AA	1.8	0.9	1.3	3.2	46	22	7	21	31
Acute-phase Inflammation	AB	0.6	1.4	1.7	2.3	1.8	11.3	1.7	8.7	10.1
Acute-phase Inflammation	AC	0.5	0.5	Nd	0.4	0.8	15.2	4.8	4.9	1.0
Acute-phase Inflammation	AD	3.3	3.3	4.2	0.9	5.4	7.8	41.1	6.0	6.2
Other	OA	Nd	0.8	Nd	0.8	3.0	6.8	4.8	3.5	5.1
Other	OB	4.7	5.3	1.6	2.6	0.3	0.6	0.6	1.3	0.5
Other Tissue Specific	SA	Nd	Nd	Nd	Nd	Nd	Nd	16	Nd	Nd



LC-MS Signal intensities
(normalized to reference standard, and proportionately scaled)

Red # denotes very severe dysregulation for at least two biomarkers for all 5 primary tumors tested

- Any oncology therapy can be evaluated by the movement of the dial towards or away from a normal/healthy characteristic pattern. So a companion **Stroma Liquid Biopsy™** biomarker panel can potentially monitor therapeutic benefit.




Developing Stroma Liquid Biopsy™
Cancer Biomarker Assays

- Proteomic Patterns for Early Detection
- Monitor Risk Factors & Wellness
- Measure Progressive Disease
- Supports New Treatment Strategies

Contact mkuruc@biotechsupportgroup.com, for a detailed whitepaper describing Stroma Liquid Biopsy™

References

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- Quail, DF., and JA Joyce. Microenvironmental regulation of tumor progression and metastasis. *Nature medicine* 19.11 (2013): 1423-1437.
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