Sistare Renal Results 8-5-02

Renal Samples
Negative = 15 samples
Renal = 11 samples

26 Total samples
10 Testing set (6 Negative and 4 Renal)
16 Training set (7 Negative and 7 Renal)
100% specificity and sensitivity

Validation with Vasculitis Positive and Negative
Classified 21/21 (100%) Vasculitis Negative as negative
Classified 16/16 (100%) Vasculitis Positive as positive

Model:

Node	Count	State	StateSum	Error	4183.515	12346.710	5396.381	10426.889	3605.287	14183.555	10286.063	3772.441
0	6	0	0	0	0.896	0.039	0.512	0.077	1.000	0.000	0.152	0.915
1	7	1	7	0	0.938	0.001	0.648	0.028	0.994	0.008	0.045	0.988
2	3	0	0	0	1.000	0.000	0.338	0.010	0.602	0.018	0.021	0.672

Sistare Dox Results 8-5-02

Dox Samples
Negative = 79 samples
Positive = 19 samples

98 Total samples
50 Testing set (39 Negative and 11Positive)
48 Training set (40 Negative and 8 Positive)
100% specificity and sensitivity

Validation with 46 unknown samples
Predicted 18/46 Positive
Predicted 28/46 Negative

Model:

Node	Count	State	StateSum	Error	14003.968	5136.478	2971.389	3631.956	8408.127	2639.668	2700.797	3995.735	3919.051	3996.903
0	1	Dox Positive	1	0	0.000	0.250	0.386	0.349	0.345	0.486	0.468	1.000	0.415	0.957
1	4	Dox Positive	3	1	0.000	0.283	0.543	0.446	1.000	0.695	0.666	0.568	0.443	0.561
4	1	Dox Positive	1	0	0.000	0.286	0.548	0.457	0.274	0.628	0.613	1.000	0.912	0.973
7	1	Dox Positive	1	0	0.000	0.368	0.682	0.540	0.310	0.827	0.789	1.000	0.783	0.986
2	1	Negative	0	0	0.000	0.175	0.644	0.461	0.886	0.885	0.847	1.000	0.491	0.946
3	13	Negative	1	1	0.000	0.418	0.831	0.636	0.241	1.000	0.966	0.668	0.608	0.662
5	8	Negative	0	0	0.000	0.420	0.776	0.638	0.919	0.959	0.925	0.959	0.644	0.938
6	18	Negative	1	1	0.000	0.432	0.812	0.648	0.485	0.994	0.951	0.923	0.657	0.901
8	1	Negative	0	0	0.000	0.378	0.764	0.609	0.980	1.000	0.966	0.702	0.589	0.703

Sistare Cardiotoxicity Results 8-5-02

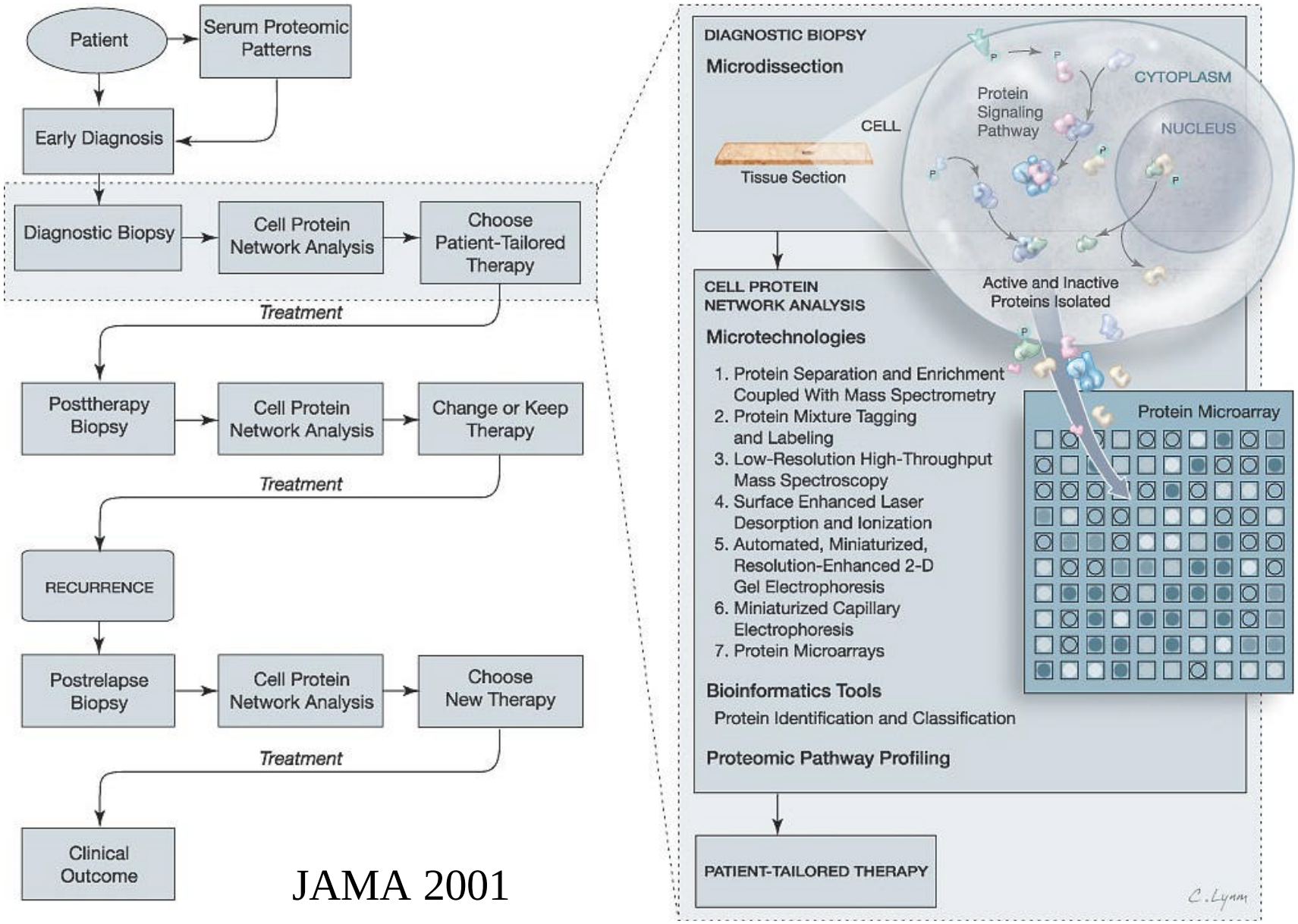
Cardiotoxicity Samples
Negative = 54 samples
Positive = 70 samples

124 Total samples
62 Testing set (29 Negative and 33 Positive)
62 Training set (25 Negative and 37 Positive)
91.6% specificity 81.5% sensitivity

Validation with 23 unknown samples
Predicted 7/23 Negative
Predicted 16/23 Positive

Model:

Node	Count	State	Error	493.592	984.298	6310.890	8526.993	577.758	577.758	7977.216	881.130	8865.985	16758.039
0	35	Cardiotox	10	0.976	0.735	0.096	0.041	0.980	0.980	0.048	0.886	0.045	0.000
1	30	Negative	6	1.000	0.574	0.101	0.059	0.753	0.753	0.083	0.661	0.087	0.000
2	45	Cardiotox	15	1.000	0.666	0.188	0.172	0.782	0.782	0.390	0.720	0.244	0.000
3	10	Cardiotox	2	1.000	0.456	0.133	0.141	0.566	0.566	0.331	0.501	0.185	0.000
4	4	Negative	1	1.000	0.807	0.251	0.274	0.897	0.897	0.667	0.858	0.351	0.000


Patient
Serum Proteomic Patterns
Early Diagnosis
Diagnostic Biopsy
Cell Protein Network Analysis
Choose Patient-Tailored Therapy
Treatment
Posttherapy Biopsy
Cell Protein Network Analysis
Change or Keep Therapy
Treatment
RECURRENCE
Postrelapse Biopsy
Cell Protein Network Analysis
Choose New Therapy
Treatment
Clinical Outcome
DIAGNOSTIC BIOPSY
Microdissection
CELL
Tissue Section
Protein Signaling Pathway
CYTOPLASM
NUCLEUS
Active and Inactive Proteins Isolated
CELL PROTEIN NETWORK ANALYSIS
Microtechnologies
1. Protein Separation and Enrichment Coupled With Mass Spectrometry
2. Protein Mixture Tagging and Labeling
3. Low-Resolution High-Throughput Mass Spectroscopy
4. Surface Enhanced Laser Desorption and Ionization
5. Automated, Miniaturized, Resolution-Enhanced 2-D Gel Electrophoresis
6. Miniaturized Capillary Electrophoresis
7. Protein Microarrays
Protein Microarray
Bioinformatics Tools
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Proteomic Pathway Profiling
PATIENT-TAILORED THERAPY
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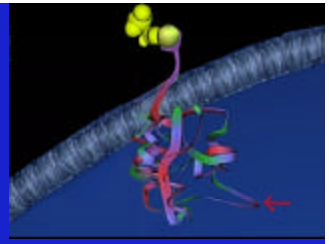
Serum Proteomic Pattern Diagnostics



- TISSUE PATHOLOGIC STATES ARE REFLECTED IN HIDDEN SERUM PROTEOMIC PATTERNS UNCOVERED USING AN ARTIFICIAL BIOINFORMATICS TOOL THAT LEARNS THE MOST FIT SOLUTION

- WE HYPOTHESIZE THAT SERUM PROTEOMIC PATTERNS ARE PRODUCT OF THE UNIQUE TUMOR-HOST MICROENVIRONMENT AND REFLECT TUMOR AND HOST INTERACTION

CURRENT STRATEGY:

TWO INDEPENDENT TRACKS:

1. SCIENTIFIC INVESTIGATION INTO SPECIFIC SOURCE AND IDENTITY OF THE CLASSIFIERS

2. NCI-BASED NATIONAL CLINICAL TRIAL ON SERUM PROTEOMIC PATTERN DIAGNOSTICS WHERE IDENTITY IS NOT NEEDED

CCR NCI Clinical Proteomics Reference Laboratory

- **Phase One:** Quality assurance, sensitivity, specificity, reproducibility, and exclusion of degraded samples, validation of initial results on larger retrospective study sets

- **Phase Two:**

A. Prospective longitudinal testing for ovarian cancer recurrence.

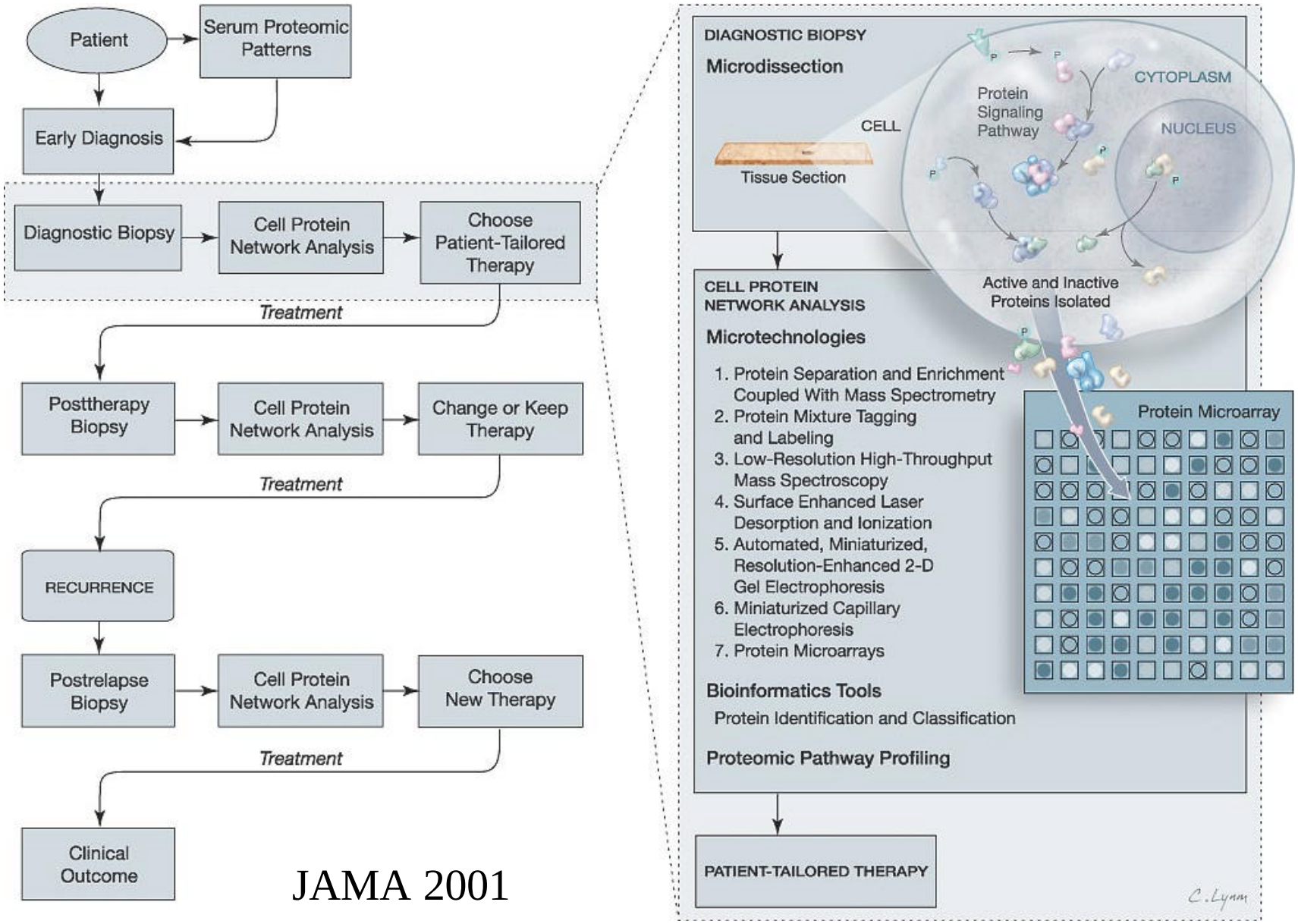
B. Classification of benign from malignant GYN disease in Women who have been diagnosed with a pelvic mass

C. High Risk Screening

- **Phase Three:** Extension to breast, prostate, lung, colon, and pancreatic cancer

Gynecologic Extramural Collaborators

- Northwestern Ovarian Cancer Early Detection Program, David Fishman
  Ovarian Cancer EDRN Consortium, David Fishman PI
- Pacific Ovarian Cancer Research Consortium, Marsha Rivken Center; Univ. Washington ovarian cancer SPORE, Nicole Urban, PI, Saul Rivken, Director
- University of Pennsylvania, George Coukos
- Memorial Sloan Kettering Cancer Center High Risk Screening Program, Ken Offit, PI
- Gynecologic Oncology Group clinical trial link newly diagnosed women, Elise Kohn PI
- Inter SPORE collaboration for screening study (ovarian cancer SPORES: U Wash, Urban confirmed; U Alabama, Partridge confirmed; Fox Chase Cancer Center, Hamilton/Daly) link for pelvic mass trial (protocol and formal SPORE collaboration mechanism in development)
- St. Bartholomew's Hospital, Ovarian Cancer Screening Program, Ian Jacobs, PI, Steve Skates, statistician
- Cancer Gene Network High Risk Women Pilot Program, through Steven Skates and CGN Steering Committee
- University of Alabama SPORE, support reference laboratory development, W. Grizzle
- Stonybrook and Long Island Jewish Hospital Consortium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Treatment
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Cell Protein Network Analysis
Change or Keep Therapy
Treatment
RECURRENCE
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Cell Protein Network Analysis
Choose New Therapy
Treatment
Clinical Outcome
DIAGNOSTIC BIOPSY
Microdissection
CELL
Tissue Section
Protein Signaling Pathway
CYTOPLASM
NUCLEUS
Active and Inactive Proteins Isolated
CELL PROTEIN NETWORK ANALYSIS
Microtechnologies
1. Protein Separation and Enrichment Coupled With Mass Spectrometry
2. Protein Mixture Tagging and Labeling
3. Low-Resolution High-Throughput Mass Spectroscopy
4. Surface Enhanced Laser Desorption and Ionization
5. Automated, Miniaturized, Resolution-Enhanced 2-D Gel Electrophoresis
6. Miniaturized Capillary Electrophoresis
7. Protein Microarrays
Protein Microarray
Bioinformatics Tools
Protein Identification and Classification
Proteomic Pathway Profiling
PATIENT-TAILORED THERAPY
C. Lynn

JAMA 2001

FDA-NCI CLINICAL PROTEOMICS PROGRAM

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