

Biomarkers for Low Back Pain: The *Right* Treatment for the *Right* Patient at the *Right* Time

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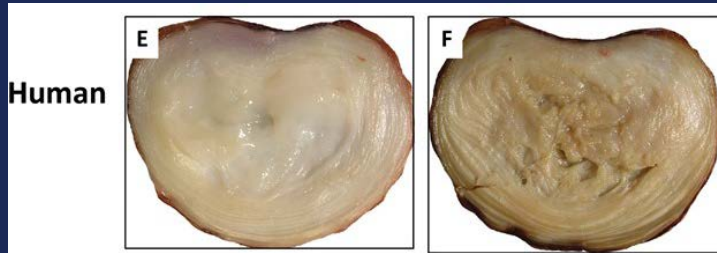


Disclosures

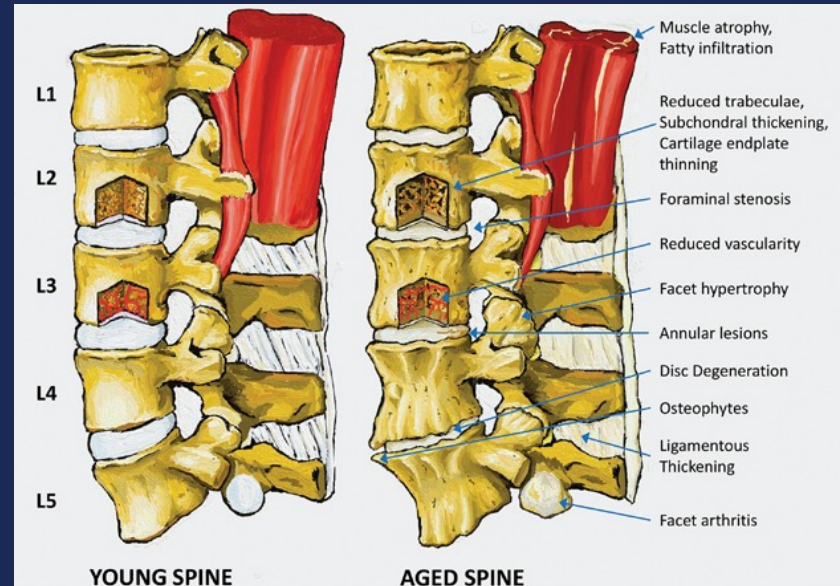
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Biomarkers for Diagnosis?

The Most Common *Diagnosis* in Low Back Pain is Disc Degeneration

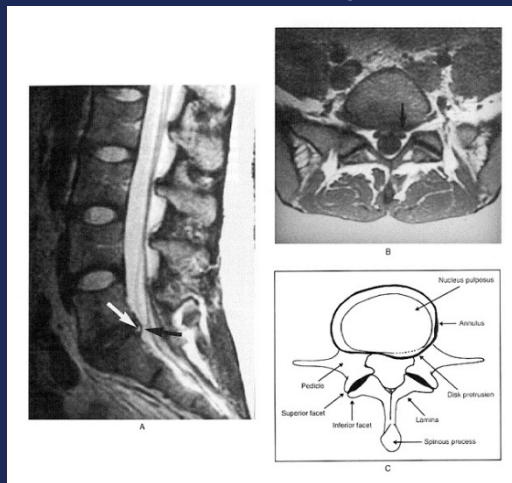


Molecular mechanisms of biological aging in intervertebral discs.
Vo et al. J Orthop Res 2016

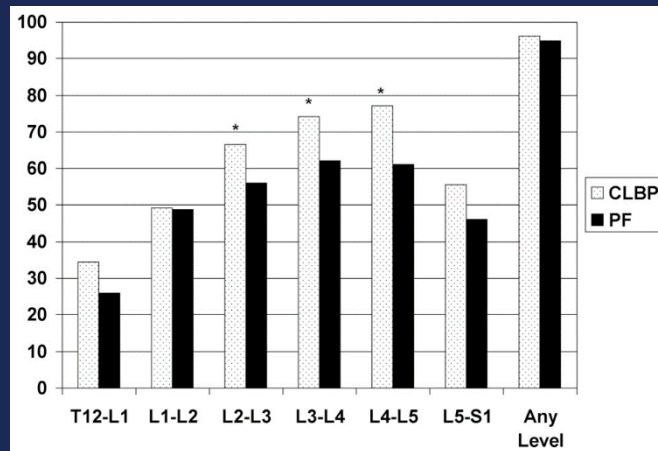


MRI as the Gold Standard?

MRI study of asymptomatic individuals with mean age 43, 52% had disc abnormality



Percent of individuals ≥ 65 with DDD

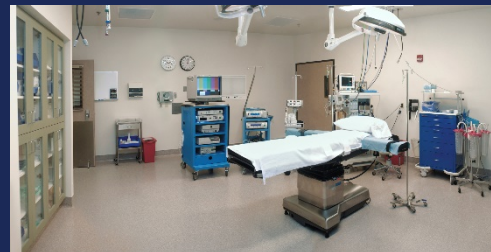
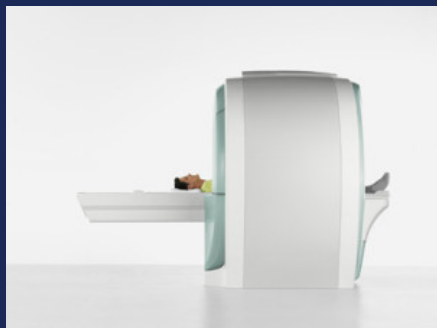


Degenerative lumbar disc and facet disease in older adults: prevalence and clinical correlates. Hicks et al. Spine 2009
 Magnetic Resonance imaging of the lumbar spine in people without back pain. Jensen et al. NEJM 1994

Imaging as a Biomarker

Lumbar Imaging in patients without indications of serious underlying conditions *does not improve* clinical outcomes

Imaging strategies for low-back pain. Chou et al. Lancet 2009



A Disc Specific Molecular Biomarker?

	Responders to Injection	Nonresponders to Injection
Fibronectin–aggrecan complex present	12	2
Fibronectin–aggrecan complex absent	1	11

Outcome of Lumbar Epidural Steroid Injection Is Predicted by Assay of a Complex of Fibronectin and Aggrecan From Epidural Lavage. Golish, et al. Spine 2011

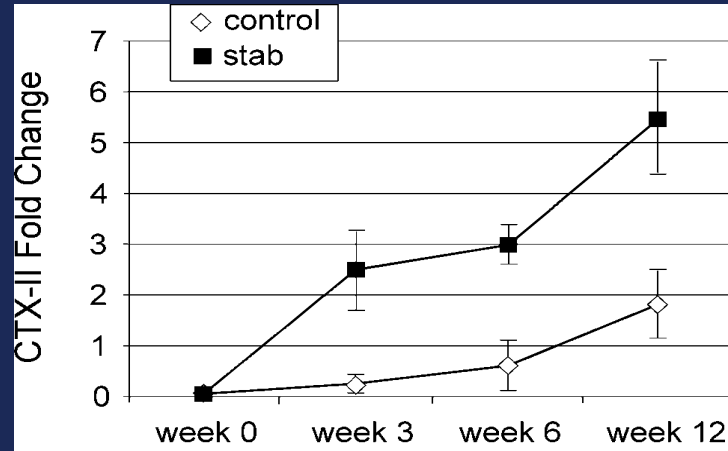
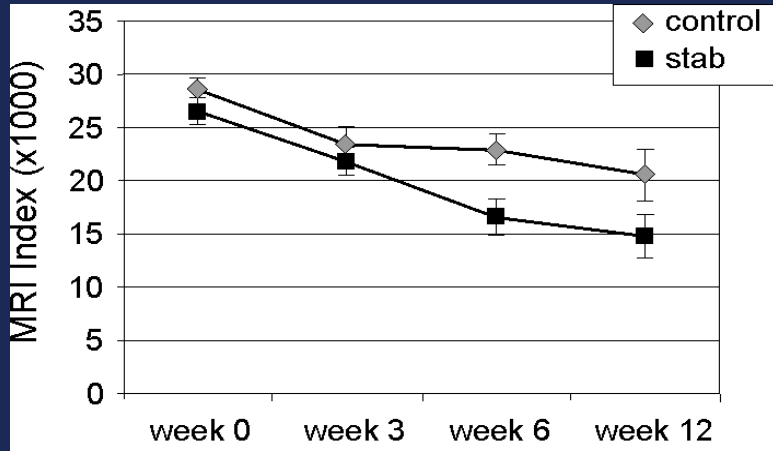
The Risks of Improper Selection

- Delay in appropriate treatment and risk of transition to chronic
 - Financial
 - Patient satisfaction
 - Risk of procedures, injections and injectates
-
- Low back pain is a multi-factorial syndrome

Existing Biomarkers Fall Short

- Imaging?
 - Not relevant to symptoms
- Pain Scores?
 - Subjective and variable relationship to function
- Assessment of Function?
 - Ceiling and floor effects make survey selection challenging
- The need: Biomarkers with increased sensitivity to change of disease activity in real time and specificity to patient phenotype and individual biology

Circulating Biomarkers May Have Greater Utility than Imaging

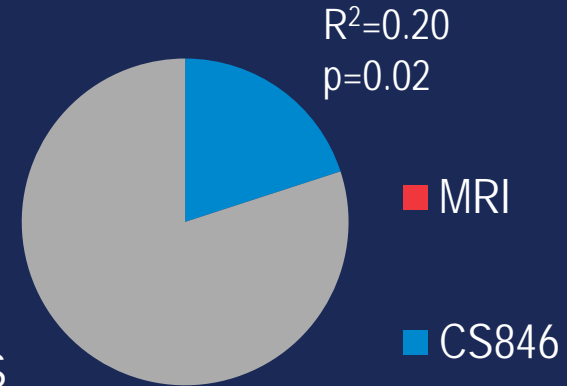
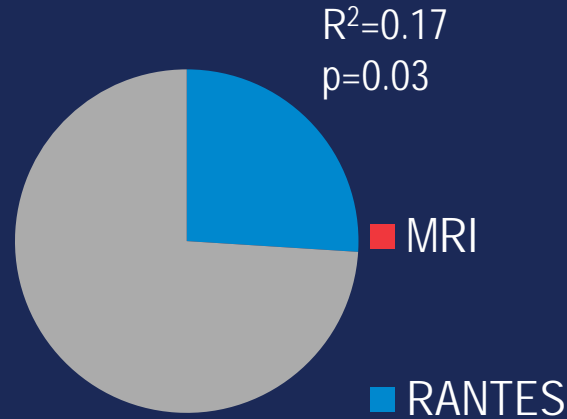
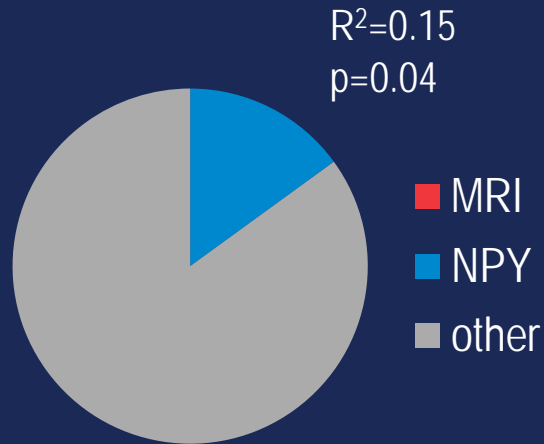


Identification of candidate serum biomarkers for intervertebral disk degeneration in an animal model.

Sowa et al. PM&R 2009

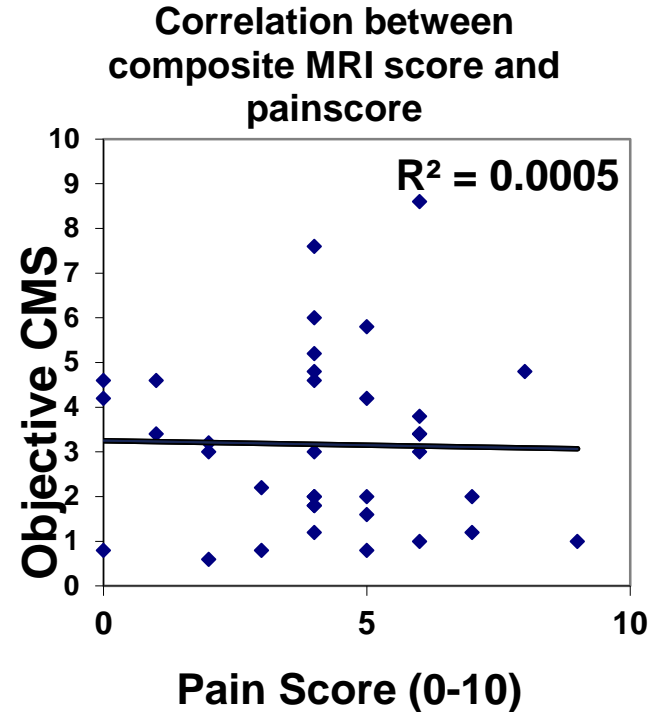
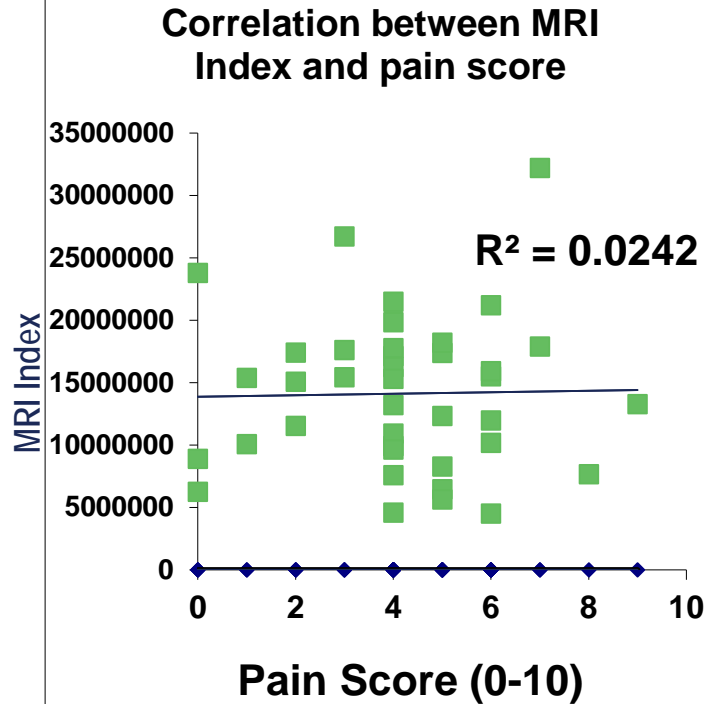
Protein Biomarkers are Associated with Pain and Pain Related Function

McGill Affective Pain Score



Associations between serum biomarkers and pain and pain related function in older adults with low back pain: a pilot study. Sowa et al. JAGS 2014

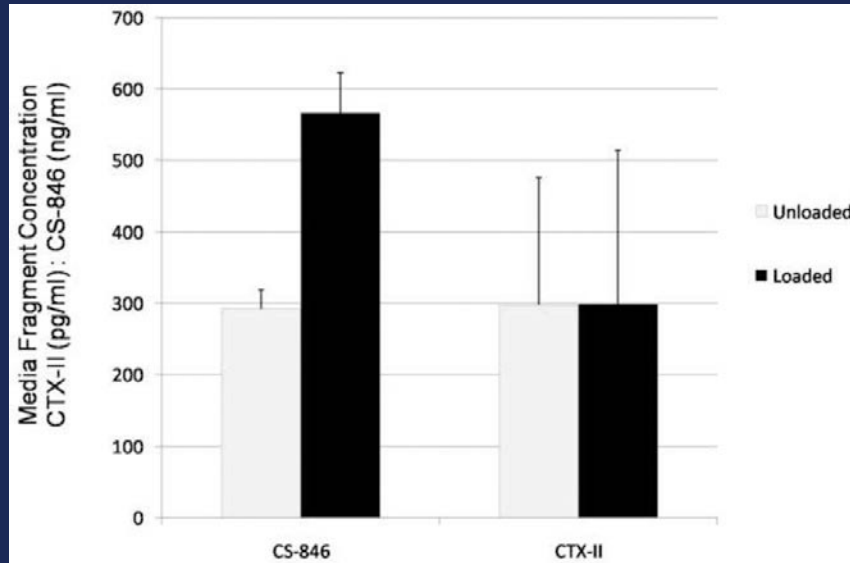
MRI does not correlate with pain or pain related function in older adults with LBP



Biomarkers to Guide Treatment?

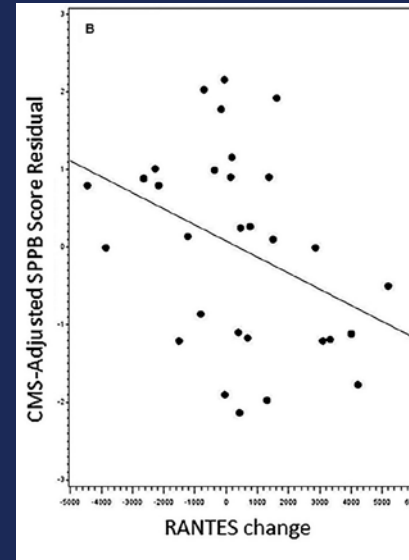
Biomarkers for Response to Exercise in LBP?

Tissue Biomarkers released in response to loading



Biological responses to flexion/extension in spinal segments ex-vivo.
Hartman et al. J Biomech 2012

Circulating changes in inflammatory markers in response to activity associated with function



Associations between serum biomarkers and pain and pain related function in older adults with low back pain: a pilot study. Sowa et al. JAGS 2014

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Circulating Biomarkers to Predict Response to Epidural Steroid Injection



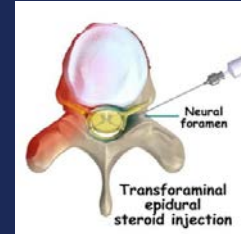
Inclusion Criteria

- Age > 18
- Low back pain > other pain
- Spinal injection performed as part of routine clinical care

Exclusion Criteria

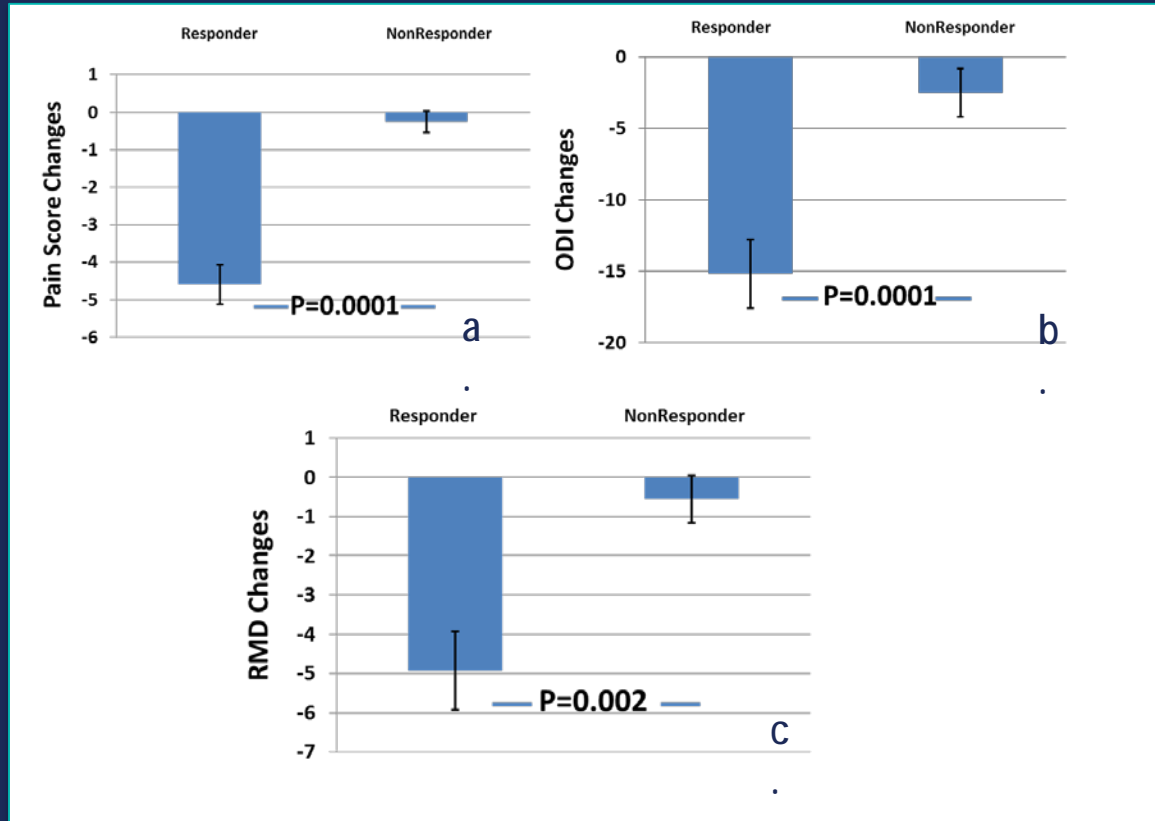
- Leg/radicular pain
- Sacroiliac joint pain
- Medical illness
- Pregnancy
- systemic inflammatory conditions or recent steroid use

Lumbar Epidural Steroid Injection
ESI n=48



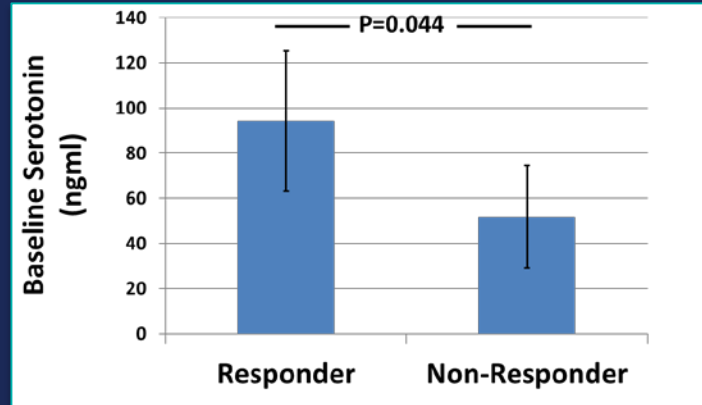
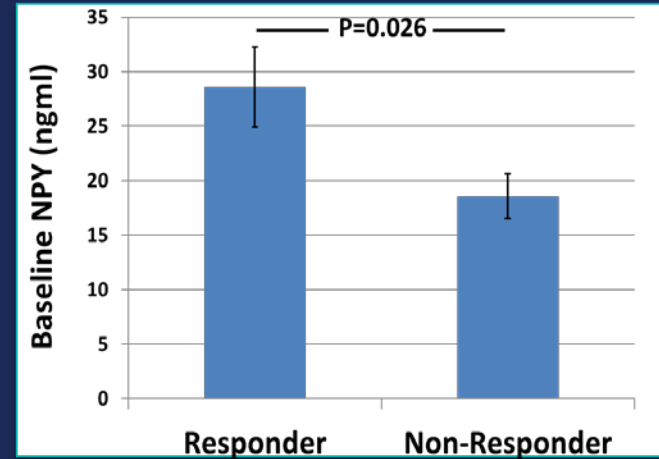
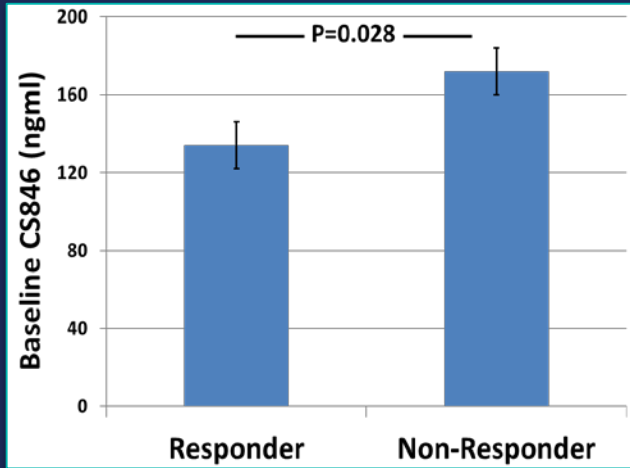
Responder defined as $\geq 50\%$ improvement in NPRS

Responders (n=17) v. Non-Responders (n=31)



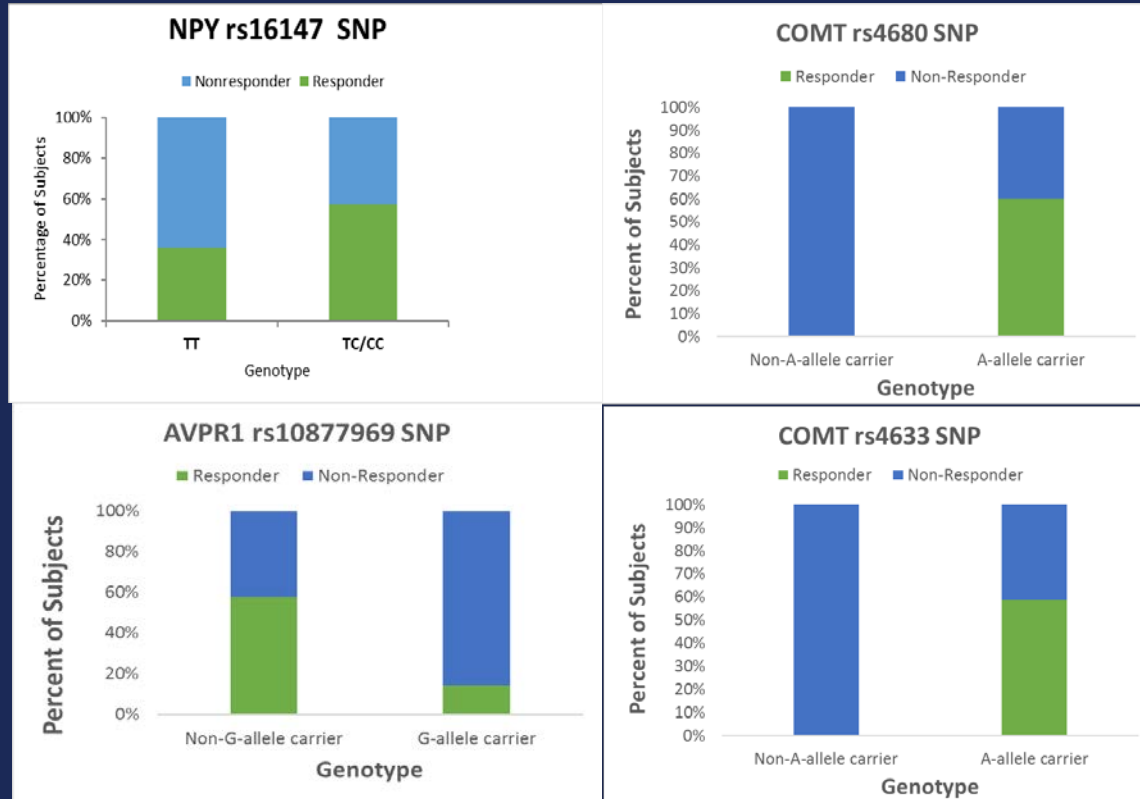
Association of protein and genetic biomarkers with response to lumbar epidural steroid injections in subjects with axial low back pain. Schaaf et al. Am J Phys Med Rehabil 2020.

Protein Biomarkers in Plasma



Association of protein and genetic biomarkers with response to lumbar epidural steroid injections in subjects with axial low back pain
Schaaf et al. Am J Phys Med Rehabil 2020.

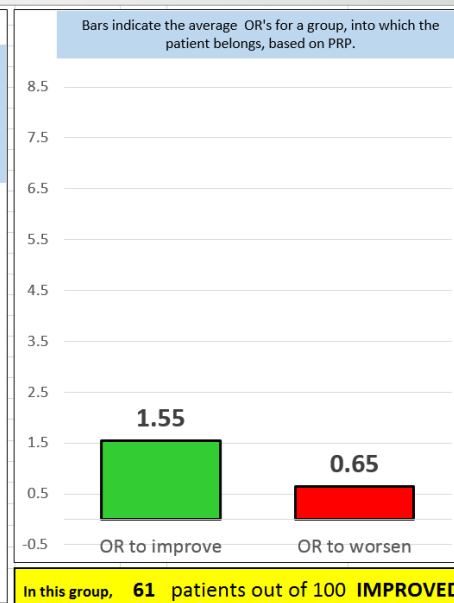
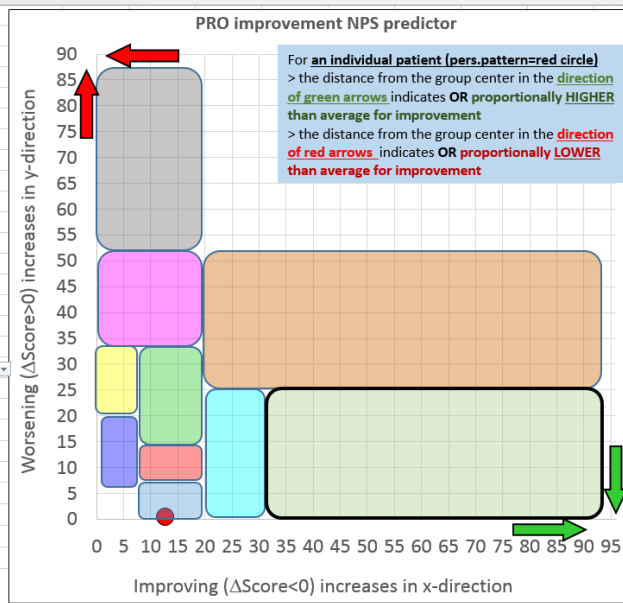
Genetic Biomarkers in Patients Undergoing ESI



Association of protein and genetic biomarkers with response to lumbar epidural steroid injections in subjects with axial low back pain
Schaaf et al. Am J Phys Med Rehabil . 2020.

Big Data using Clinical Biomarkers to Predict Response

PRE-score	40-60
alcohol	No
tobacco	No
ILL_drug	No
MuscleRelaxant	No
Opioid drug use	No
non-Steroidal anti-inflammatory drugs	No
Antidepressant use	No
Seizure	No
Diabetes	No
Congestive heart failure (CHF)	No
Fibro Myalgia	No
Irritable bowel syndrome (IBS)	No
Rheumatoid Arthritis (RA)	No
CTD	No
Hypothyroidism (HypoTHR)	No
Thyroid diorder (ThrDisord)	No
Anxiety	No
Depression	No
Sleep Apnea	No
Post-traumatic stress disorder (PTSD)	No
Set all to No	
Relative correctness (gray region=100.0) is	30.800
	expected



UPMC Clinical Analytics
 Oscar Marroquin, Steven Koscomb, Petr Pancoska, Kevin Quinn, Susie Ho

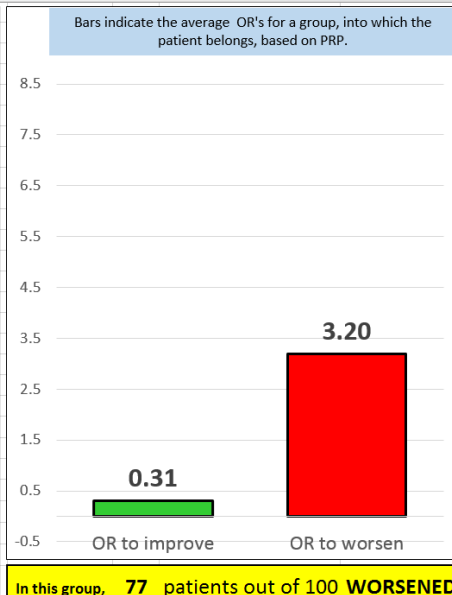
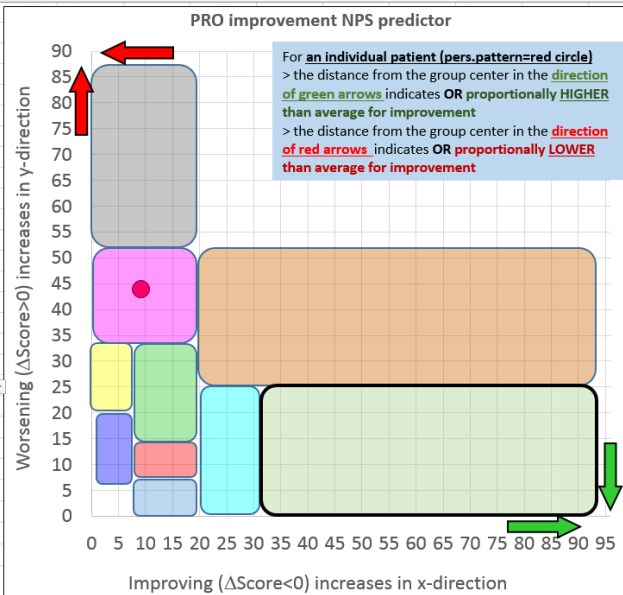
The *million small victories* Institute.

UPMC Rehabilitation Institute

PRE-score	40-60
alcohol	No
tobacco	No
ILL_drug	No
MuscleRelaxant	Yes
Opioid drug use	Yes
non-Steroidal anti-inflammatory drugs	Yes
Antidepressant use	Yes
Seizure	No
Diabetes	No
Congestive heart failure (CHF)	No
Fibro Myalgia	Yes
Irritable bowel syndrome (IBS)	Yes
Rheumatoid Arthritis (RA)	No
CTD	No
Hypothyroidism (HypoTHR)	No
Thyroid disorder (ThrDisord)	No
Anxiety	No
Depression	No
Sleep Apnea	No
Post-traumatic stress disorder (PTSD)	No

Set all to No

Relative correctness (gray region=100.0) is **78.200**
expected



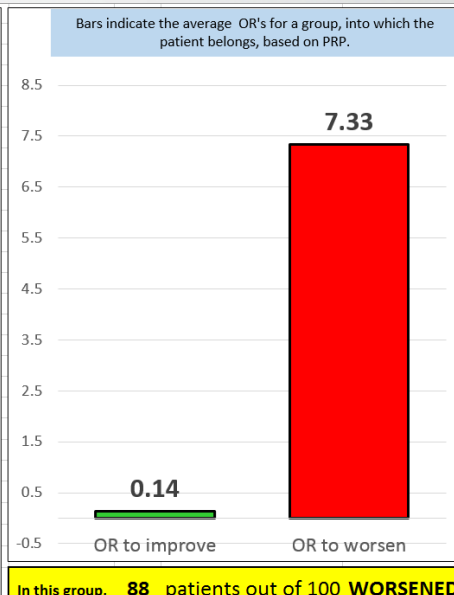
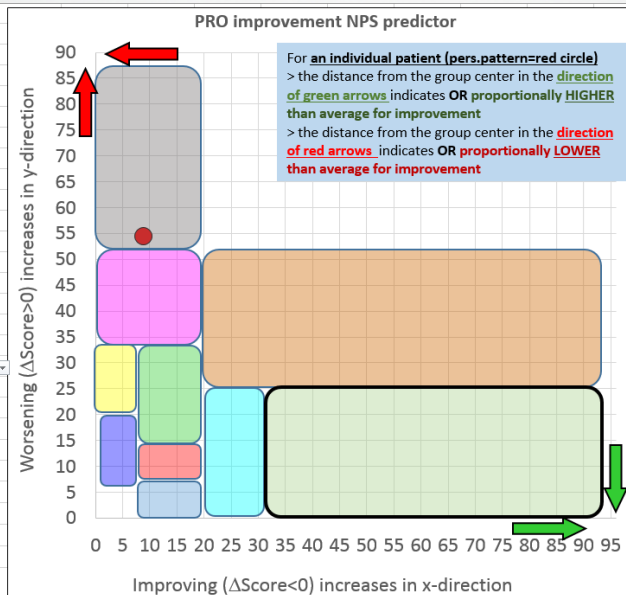
The *million small victories* Institute.

UPMC Rehabilitation Institute

PRE-score	40-60
alcohol	No
tobacco	No
ILL_drug	No
MuscleRelaxant	Yes
Opioid drug use	Yes
non-Steroidal anti-inflammatory drugs	Yes
Antidepressant use	Yes
Seizure	No
Diabetes	No
Congestive heart failure (CHF)	No
Fibro Myalgia	Yes
Irritable bowel syndrome (IBS)	Yes
Rheumatoid Arthritis (RA)	No
CTD	No
Hypothyroidism (HypoTHR)	No
Thyroid disorder (ThrDisord)	No
Anxiety	Yes
Depression	Yes
Sleep Apnea	No
Post-traumatic stress disorder (PTSD)	No

Set all to No

Relative correctness (gray region=100.0) is **61.500**
expected

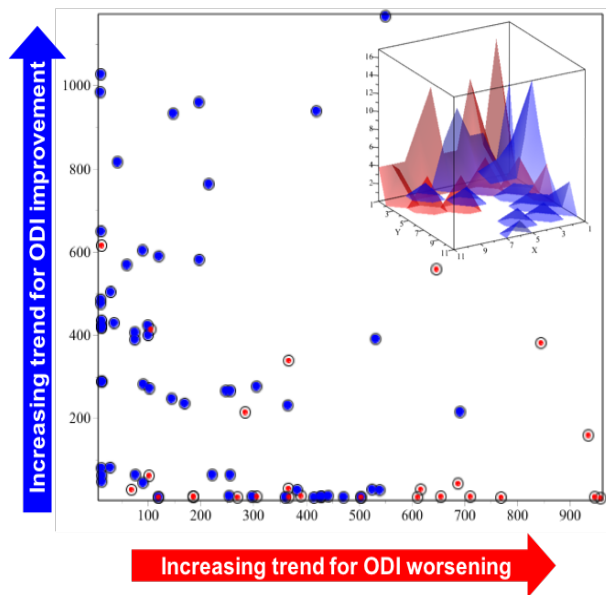


The *million small victories* Institute.

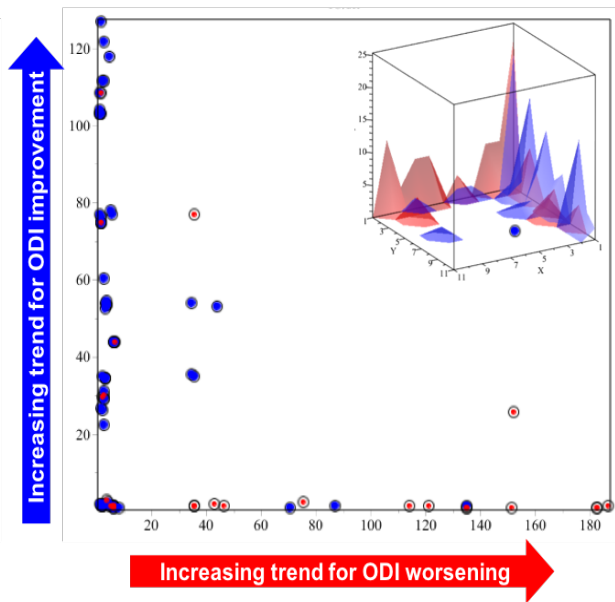
UPMC Rehabilitation Institute

Improved Phenotyping with Biomarkers from Multiple Domains

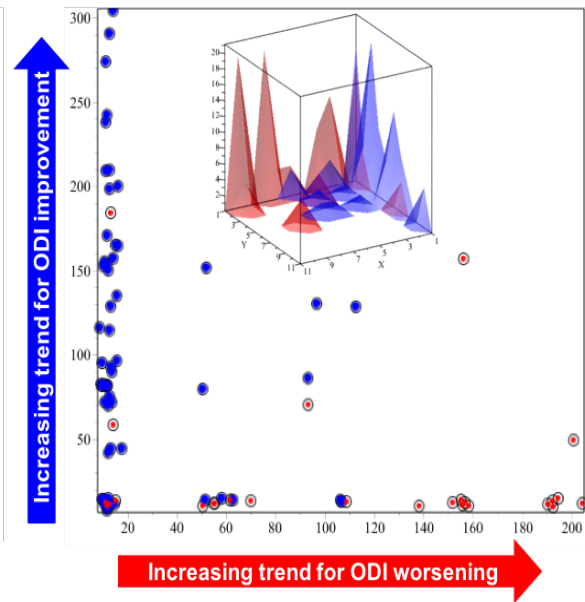
A) Clinical Data Only



B) SNP Data Only



C) Clinical & SNP Data



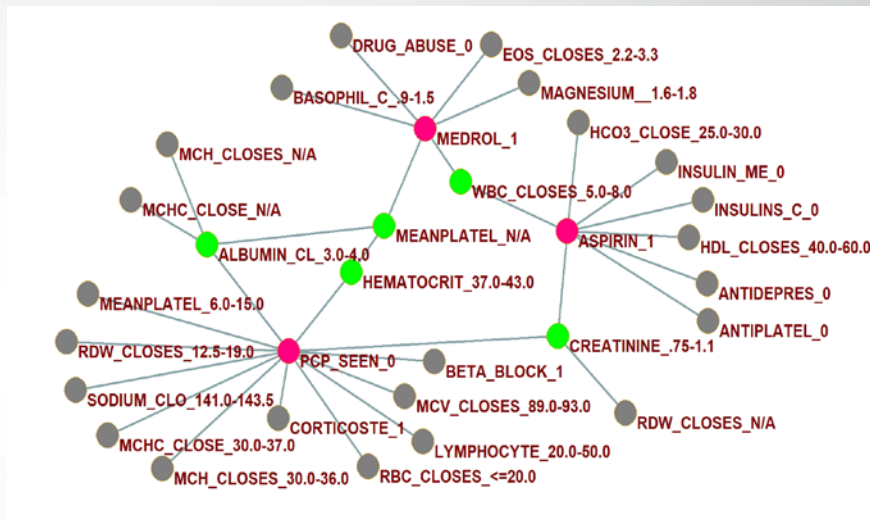
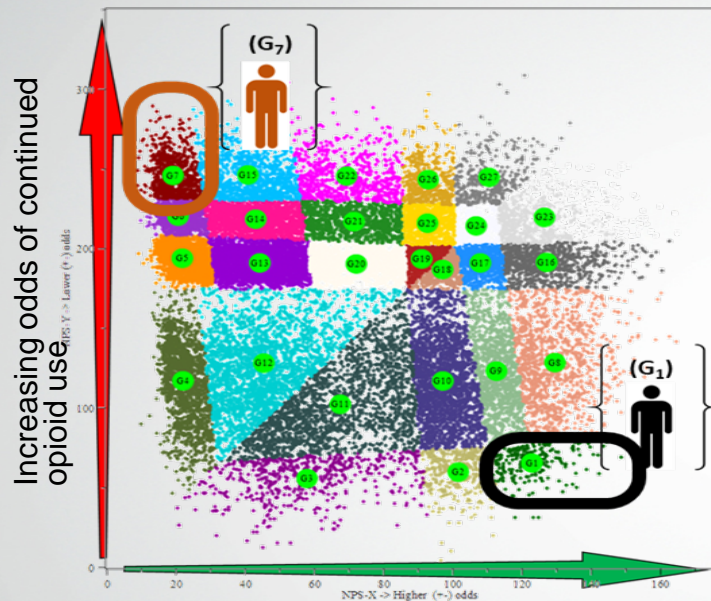
Biomarkers to Phenotype LBP Types

Differences in Relationships with Pain and Inflammatory Biomarkers

	McGill Affective	Pain Scale	Depression	Gait speed	SPPB	FABQ
NPY	0.23*	0.04	0.20*	0.00	0.01	0.22*
RANTES	0.03	0.15*	0.04	0.19*	0.15*	0.03

*Combinations of Biomarkers demonstrated larger significant associations

Network Phenotyping Strategy

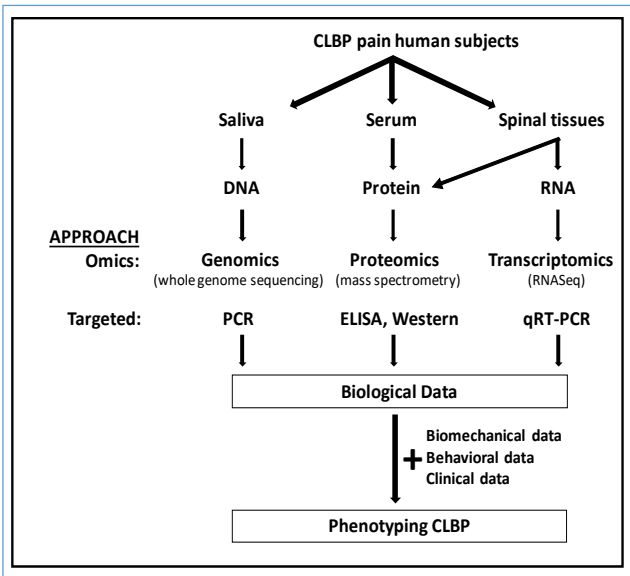


Funded by the Beckwith Foundation

Oscar Marroquin, Petr Pancoska, Ajay Wasan, Howard Gutstein

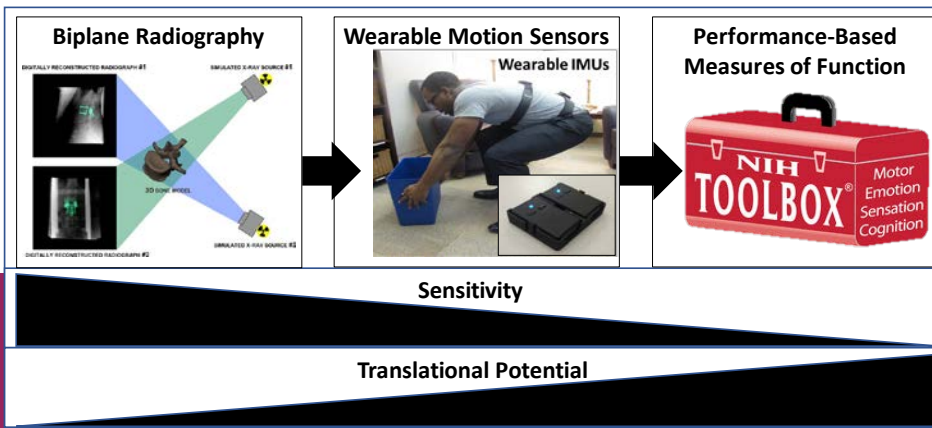
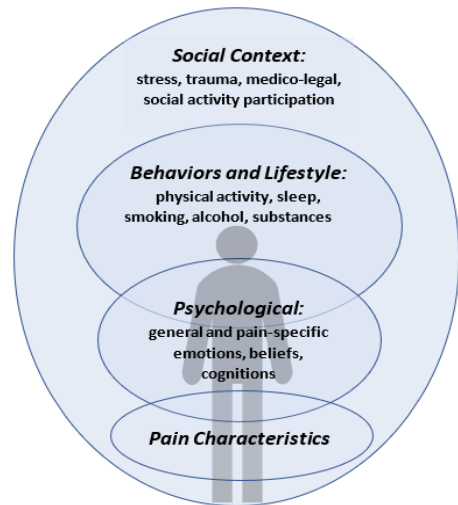
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NIH/NIAMS U19AR076725

The Person with Pain: Social, Behavioral, and Psychological Context



NIH
HEAL
INITIATIVE

BACPAC





The right *treatment*, for the
right *patient*, at the right *time*

Development of phenotyping
capabilities that includes clinical history,
exam, radiographic findings and
personal biology



