UNIVERSITY of MARYLAND
SCHOOL OF NURSING

PAIN AND TRANSLATIONAL
SYMPTOM SCIENCE DEPARTMENT

UNIVERSITY of MARYLAND
CENTER TO ADVANCE CHRONIC PAIN RESEARCH

Use of –omics to identify biomarkers for pain research and clinical practice

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Distinguished University Professor

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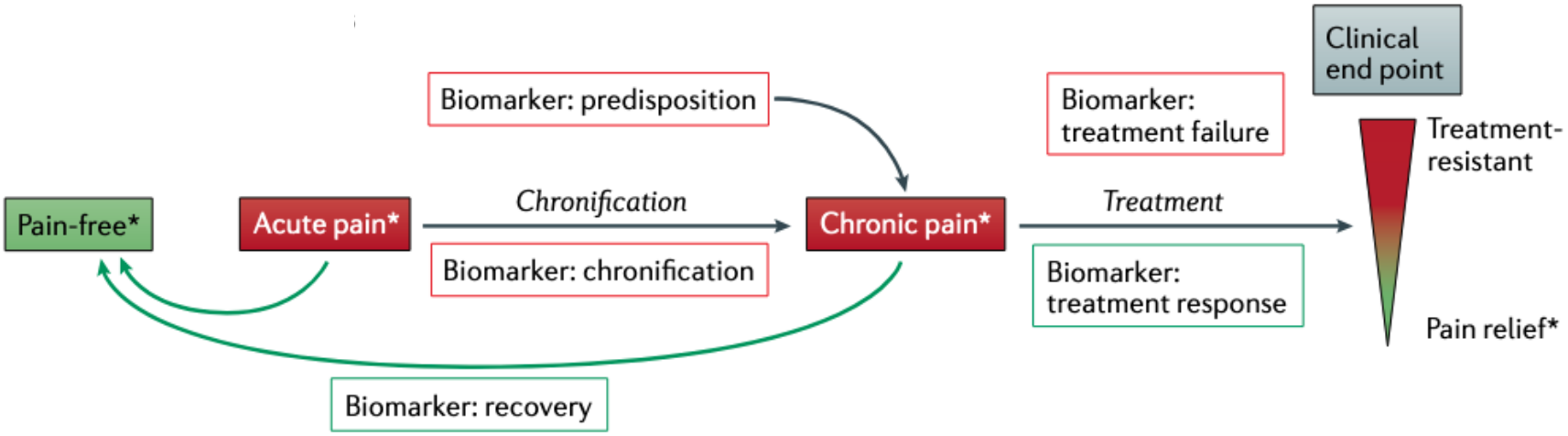
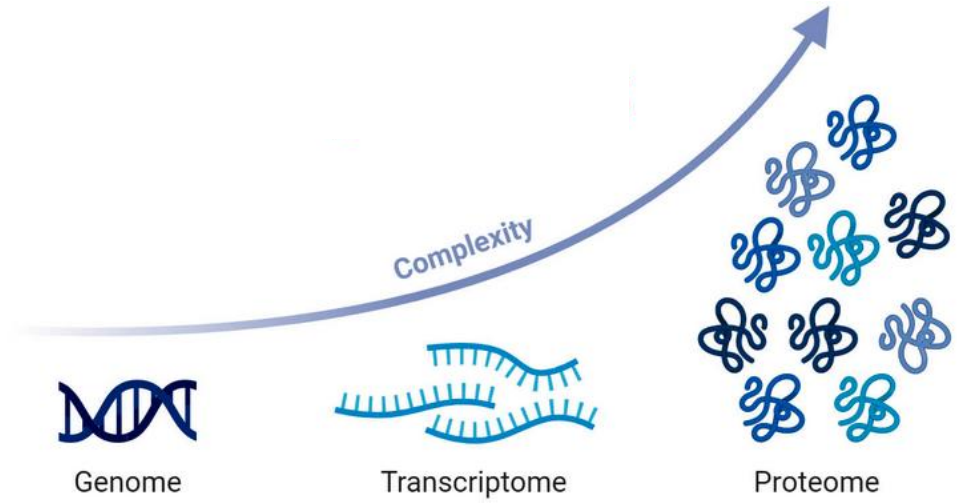
High prevalence of chronic pain combined with low efficacy of current treatment regimens and the opioid crisis support biomarker identification

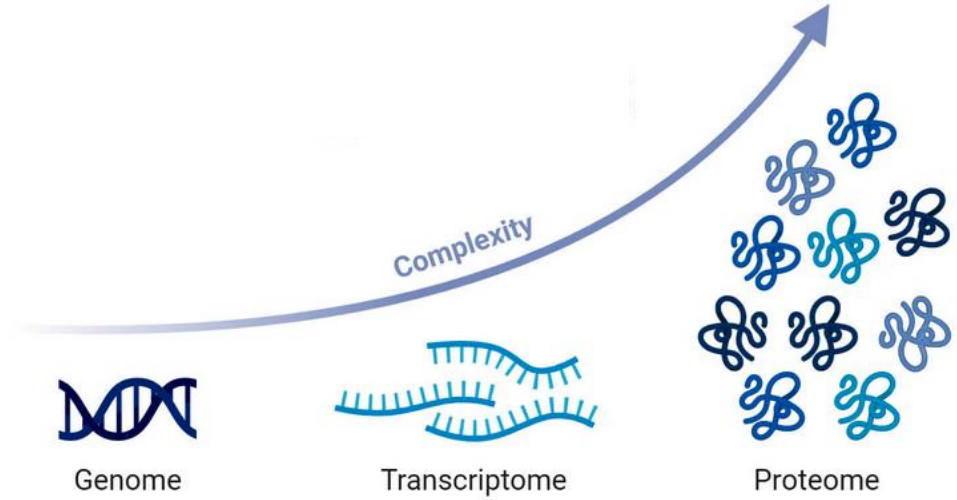


Davis et al., 2020 Consensus Statement, *Nature Rev Neurology*

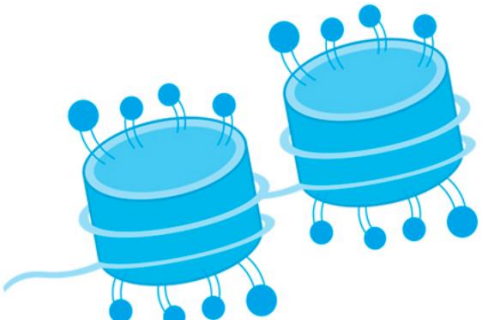
-Omics biomarkers



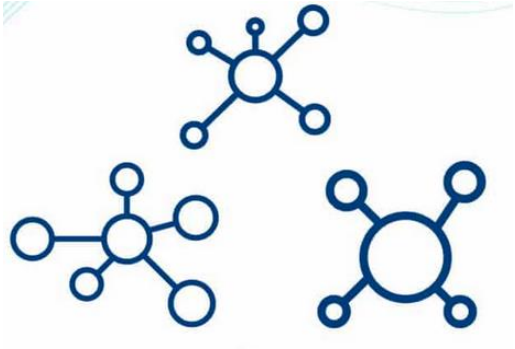
-Omics biomarkers can be assayed from a variety of human sources



Microbiome

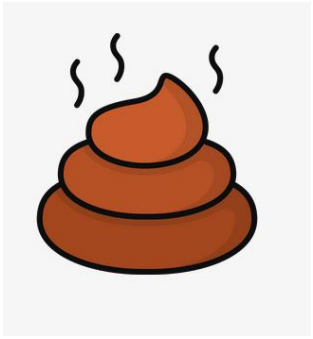


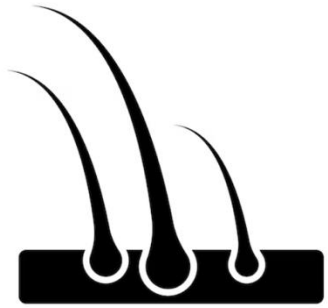
Epigenomics

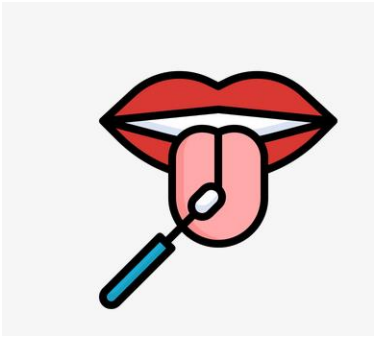


Metabolomics

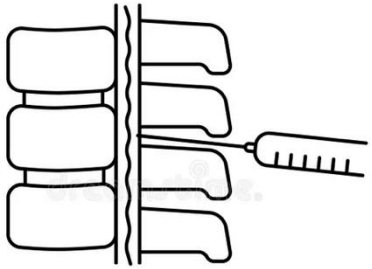
Lipidomics

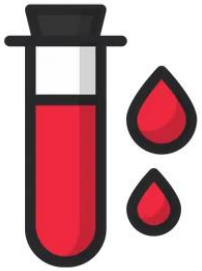






Sources of –omics biomarkers in human





Robust phenotyping is critically important in biomarker development—example from current cLBP study

	BL	6 Wks	8 Wks	10 Wks	12 Wks	16 Wks	20 Wks	24 Wks	52 Wks	18 Mos	2 Yrs
Sociodemographic Data	X										
Clinical Data	X	X			X			X	X		X
Brief pain Inventory	X	X	X	X	X	X	X	X	X	X	X
McGill Pain Questionnaire – Short Form	X	X	X	X	X	X	X	X	X	X	X
Coping Strategies Questionnaire	X	X	X	X	X	X	X	X	X	X	X
Kohn Reactivity Scale	X	X	X	X	X	X	X	X	X	X	X
Profile of Mood States	X	X	X	X	X	X	X	X	X	X	X
Roland Disability Questionnaire	X	X	X	X	X	X	X	X	X	X	X
Perceived Stress Scale	X	X	X	X	X	X	X	X	X	X	X
Neurophysiological Testing	X	X			X			X	X		X
Blood Draw	X	X			X			X	X		X

BL = Baseline; Wks = Weeks; Mos = Months; Yrs = Years; Orange = Clinical Testing Visit

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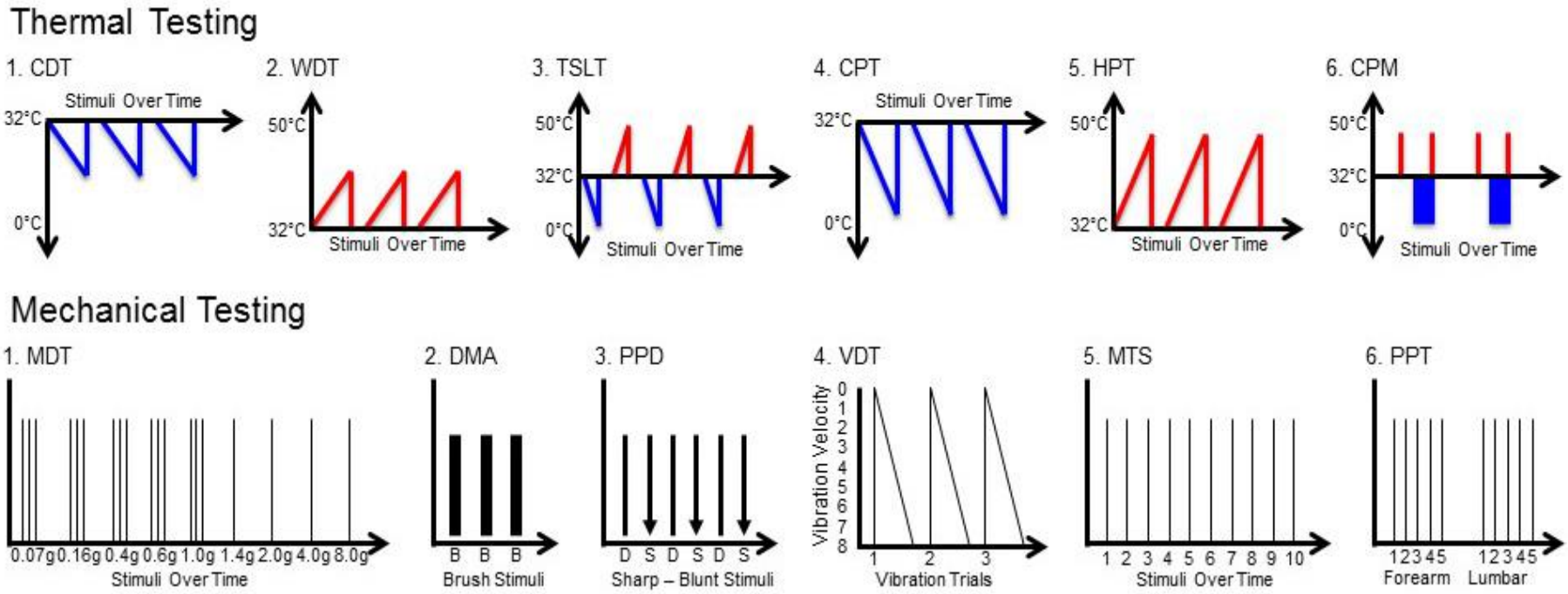
Neurophysiological testing (QST)



CDT=cool detection threshold; WDT=warmth detection threshold; TSLT=thermal sensory limen test; CPT=cold pain threshold; HPT=heat pain threshold; MDT=mechanical detection threshold; DMA=dynamic mechanical allodynia; PPD=pin prick detection; VDT=vibration detection threshold; MTS=mechanical temporal summation; PPT=pressure pain threshold; CPM=conditioned pain modulation.

Based upon the German Research Network on Neuropathic Pain (Rolke et al., 2006a; Rolke et al., 2006b)

Phenotype data from cLBP study

	Baseline	Baseline	Baseline	6 months	
	Normal (healthy controls) N = 21	**Acute N = 11**	**Chronic-baseline (T1) N = 13**	**Chronic- 6 months (T5) N = 19**	**P-value**
Age, mean (SD)	30.9 (13.9)	34.4 (9.1)	38.5 (8.4)	38.7 (9.0)	0.184
Gender					0.993
Male (%)	9 (42.9)	5 (45.5)	6 (46.2)	9 (47.4)	
Female (%)	12 (57.1)	6 (54.4)	7 (53.8)	10 (52.6)	
Race					<0.001
White (%)	12 (57.1)	6 (56.0)	6 (46.2)	8 (42.1)	
Black (%)	1 (4.8)	3 (27.0)	7 (53.8)	11 (57.9)	
Other (%)	8 (38.1)	2 (18.0)	0 (0.0)	0 (0.0)	
Pain score right now (0–10) mean (SD)	0 (0.0)	2.9 (0.9)	5.5 (2.5)	5.7 (2.8)	<0.001
Pain average score (0–10) mean (SD)	0 (0.0)	3.4 (1.6)	5.2 (2.0)	5.1 (2.4)	<0.001
Heat pain tolerance mean (SD)	43.3 (3.7)	40.5 (4.6)	40.0 (3.0)	39.5 (3.3)	0.008
Pain medication (opioid) mean (0 = no, 1 = yes) (SD)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	—
Pain medication (NSAID/Tylenol) mean (0 = no, 1 = yes) (SD)	0 (0.0)	0.64 (0.50)	0.23 (0.44)	0.32 (0.48)	<0.001

[a]p-values were calculated from ANOVA or Chi-square test(s), whenever applicable

Dorsey et al., 2019

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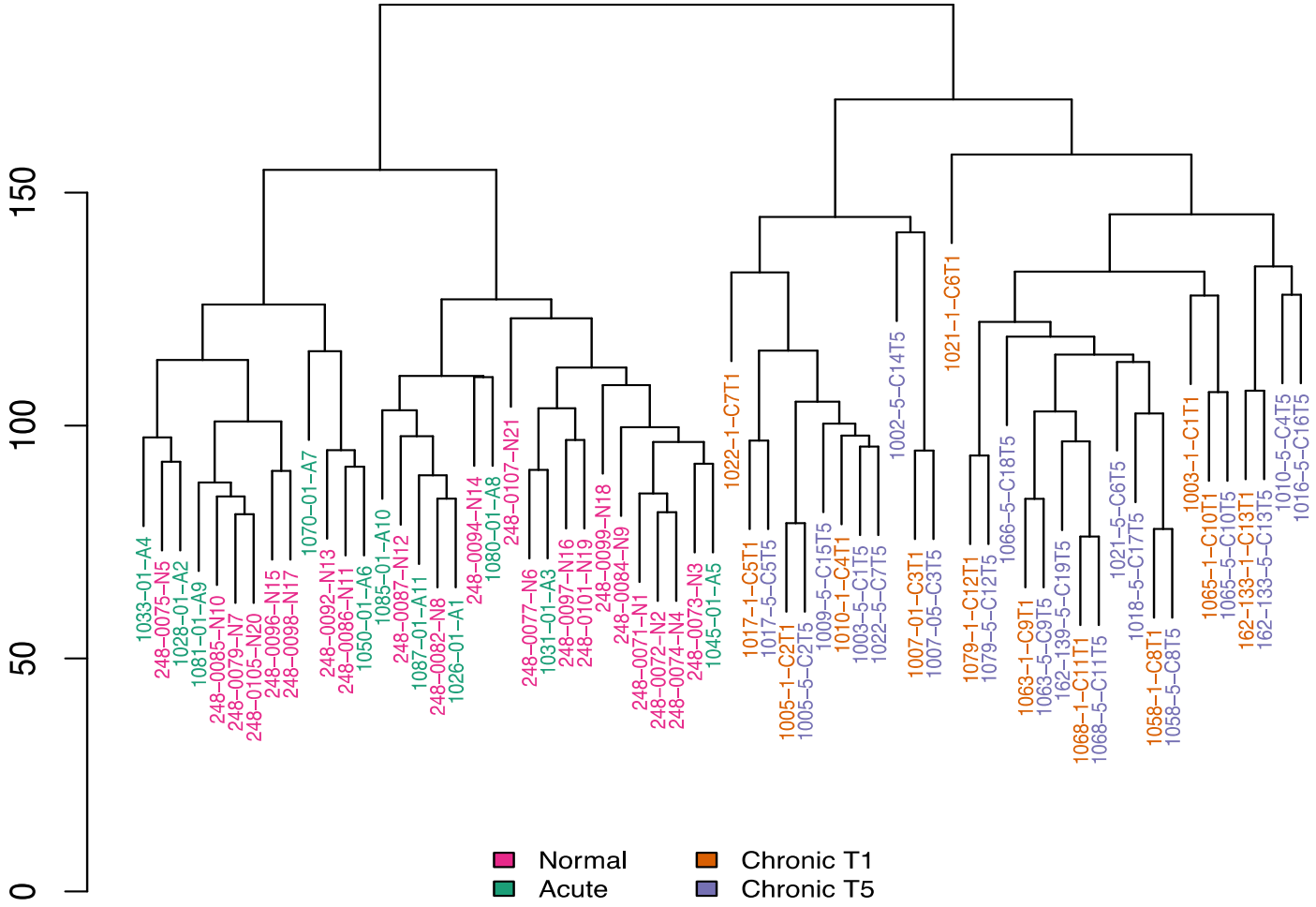
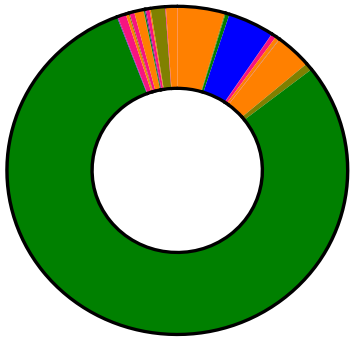
Dorsey et al., 2019

Transcriptomic profiles clustered groups into two groups (HC/Acute baseline) and cLBP (baseline/6 months)

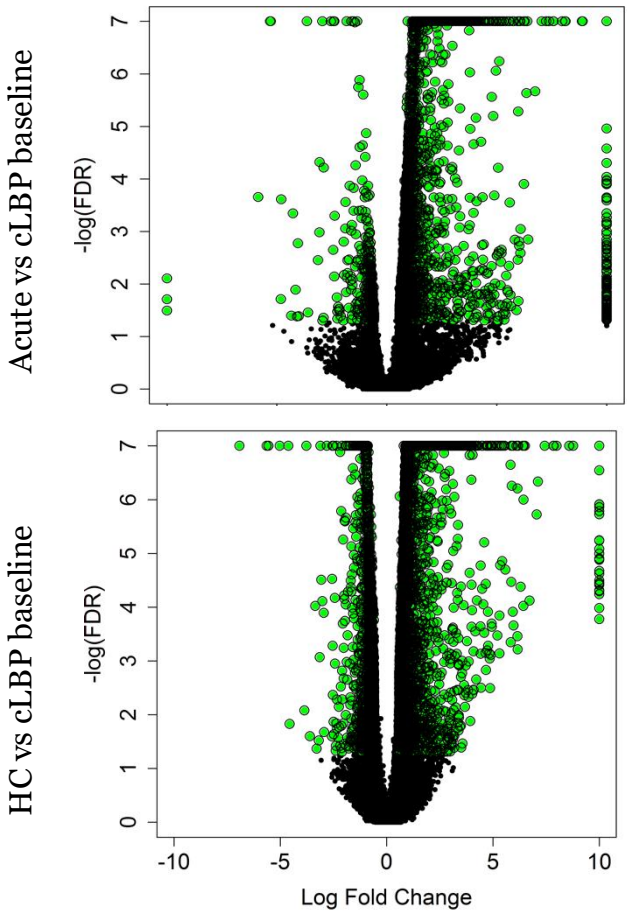


Majority of the transcripts are protein coding

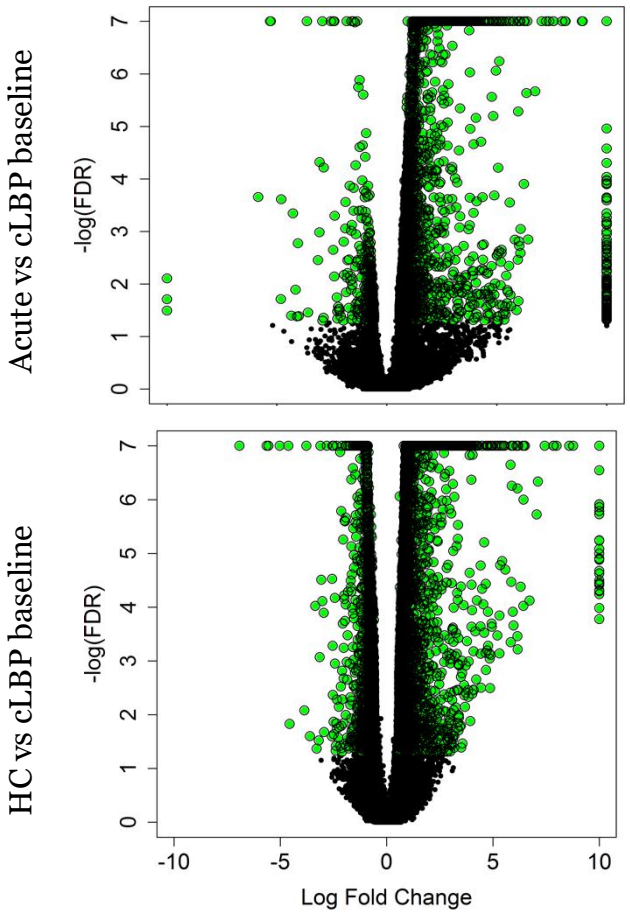


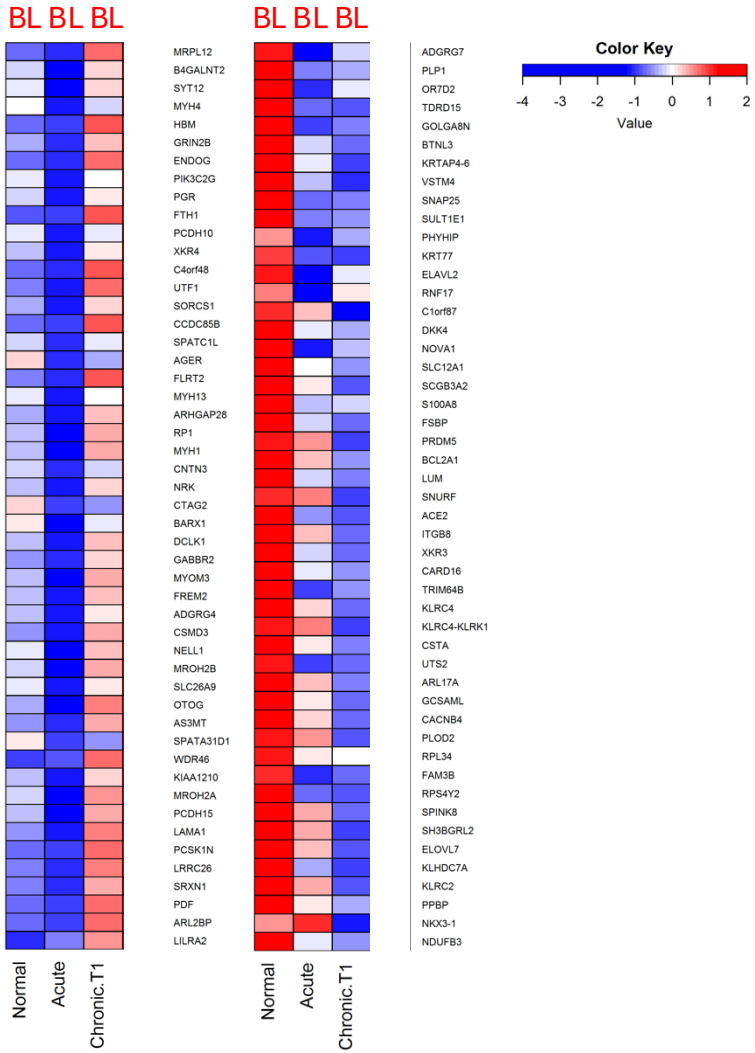
- 2 3prime_overlapping_ncRNA
- 252 antisense
- 5 IG_C_gene
- 20 IG_V_gene
- 248 lincRNA
- 1 macro_lncRNA
- 26 miRNA
- 20 misc_RNA
- 2 Mt_rRNA
- 1 polymorphic_pseudogene
- 196 processed_pseudogene
- 39 processed_transcript
- 4486 protein_coding
- 1 pseudogene
- 4 rRNA
- 44 sense_intronic
- 14 sense_overlapping
- 6 snoRNA
- 25 snRNA
- 50 TEC
- 2 TR_C_gene
- 6 TR_J_gene
- 1 TR_J_pseudogene
- 6 TR_V_gene
- 18 transcribed_processed_pseudogene
- 6 transcribed_unitary_pseudogene
- 77 transcribed_unprocessed_pseudogene
- 4 unitary_pseudogene
- 60 unprocessed_pseudogene

Transcriptomic profiles between HC and cLBP patients at baseline different than between acute LBP patients compared with cLBP participants at baseline

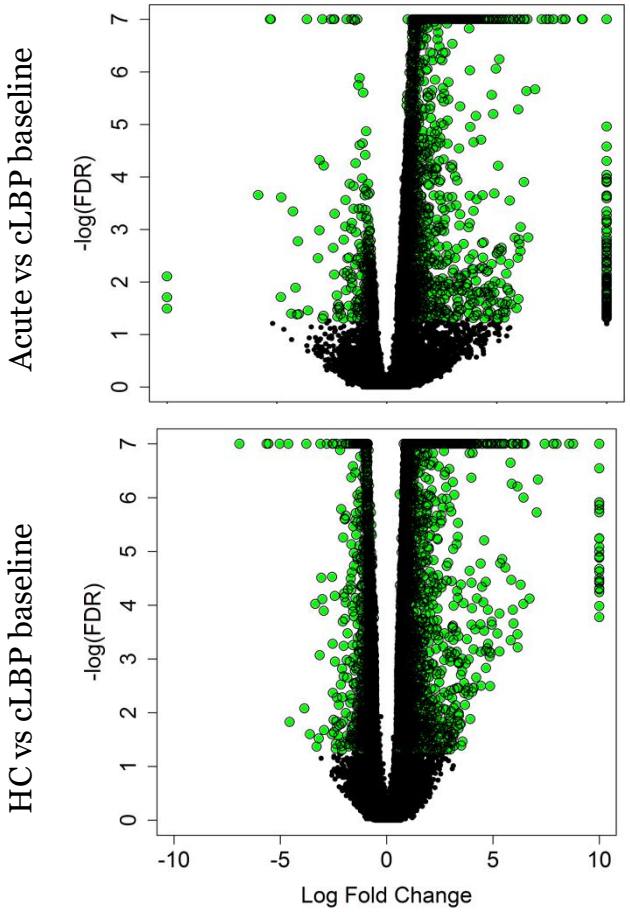


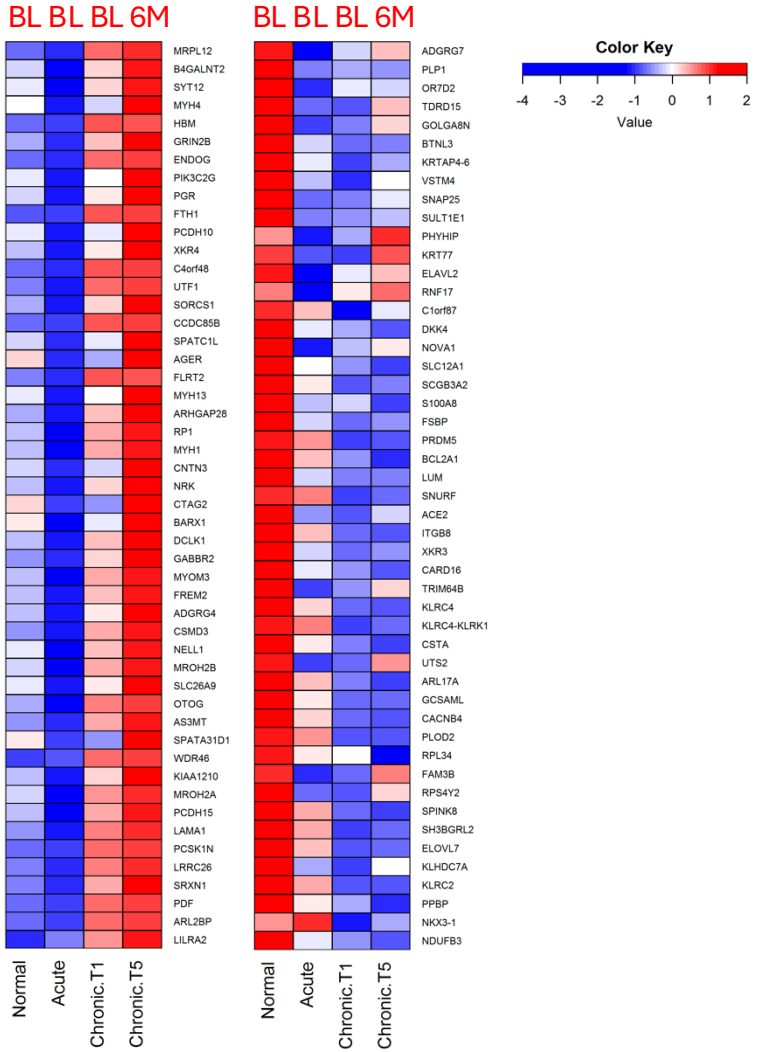
Transcriptomic profiles differ across the four phenotype groups by the two clusters, and most do not change over time





Transcriptomic profiles differ across the four phenotype groups by the two clusters (HC/aLBP vs Baseline/6mo cLBP)

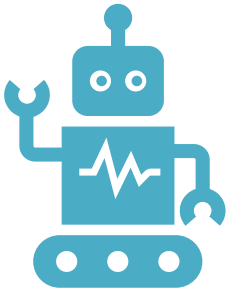




What are the pressing issues for –omics to identify biomarkers

1. Most studies (except OPPERA) don't profile –omics prior to injury/event
2. Most studies use one –omics method and not multi-modal approach
3. Most studies are cross-sectional rather than longitudinal
4. Which tissues/cells make most sense to profile (e.g., blood vs. PBMCs vs EVs)
5. Which method of profiling (e.g., whole transcriptome vs. single cell; others)

Additional future considerations



Computational infrastructure and informatics expertise in Machine Learning (ML)/Artificial Intelligence (AI) methods to analyze phenotype and –omics data together for predictive purposes;

Large sample size studies as described (cLBP study) or smaller sample sizes using the N of 1 approach as an example.

Thank you!

Looking forward to the discussion with the panel and audience members!