UNIVERSITY OF CALGARY

FACULTY OF MEDICINE

Department of Medicine
2500 University Drive NW
Calgary, AB, Canada T2N 1N4
ucalgary.ca

October 21, 2023

Myositis Canada
#103, 7724 Bowness Rd NW
Calgary AB T3B 0H1

RE: Final Progress Report for SOAR Project

Dear Myositis Canada,

We would like to express our gratitude once again for your support and funding of our research project, SOAR: Sporadic Inclusion Body Myositis NOvel Autoantibody and Biomarker Research. While this marks the final report, it does not signify the end of our research efforts aimed at advancing our understanding of sporadic inclusion body myositis (sIBM). In fact, we are just beginning to embark on many new and exciting research projects that have emerged from SOAR!

Through SOAR, we have made several important findings that have been presented at six rheumatology conferences, including two national meetings. Additionally, we were recently invited to give an oral presentation at the upcoming international American College of Rheumatology conference in San Diego in November. We have consistently acknowledged the funding support we received from Myositis Canada during each of these presentations.

As a result of this work, we have further developed our research ideas and initiated several new projects. We have secured an additional $32,000 in peer-reviewed funding and $50,000 from industry sources, with three grant applications requesting $1,000,000 for these projects currently under consideration. Importantly, our team has significantly expanded in size and expertise over the last

several years, including multiple rheumatologists, neurologists, a rheumatology resident, and graduate students. This growth has been made possible through your support, and we would not have achieved this level of success without it!

Finally, I would like to inform the board of the context of my research over the past two years. During this time, I was away for two maternity leaves as my family grew. Although I was allowed time off for clinical work, I specifically chose to continue to research work on this project to ensure that it was completed on time and met all the proposed deliverables for the grant.

Specific Aims:

Aim 1 (COMPLETED): We performed a comprehensive myositis autoantibody panel including novel biomarkers anti-NT5c1A, anti-mitochondrial (AMA), anti-Ro52/TRIM21, and anti-VCP antibodies in sIBM patient sera. While we demonstrated that the seronegative gap (patients with no autoantibodies) in sIBM decreased, particularly with the addition of anti-NT5c1A, anti-mitochondrial (AMA), anti-Ro52/TRIM21 antibodies, a significant gap remains. These results have been presented at multiple conferences and summarized in a manuscript that is in submission to Annals of Rheumatic Diseases.

Aim 2 (COMPLETED): We determined that sIBM can be differentiated from other types of myositis using artificial intelligence algorithms to identify unique patient phenotypic clusters based on established and novel myositis autoantibodies. Different autoantibody clusters were helpful in differentiating sIBM patients from other types of myositis. These results have been presented at multiple conferences and summarized in a manuscript that is in submission to Annals of Rheumatic Diseases.

Students

2023-Present **Farbod Moghaddam,** Undergraduate Summer Student, University of Calgary
Project Title: “SOAR UP: Sporadic Inclusion Body Myositis NOvel Autoantibody and Biomarker Research Utilizing Proteome Microarray"
Oral Presentation at the 2022 McCaig Summer Student Symposium
Poster Presentation at the 2022 Snyder Summer Undergraduate Research
Abstract submission to the 2023 Global Conference on Myositis in progress

2022-Present **Jenny Wei**, Undergraduate Summer Student, University of Toronto
Topic: Sporadic Inclusion Body Myositis Novel Biomarkers and Machine Learning

Recipient of the 2022 Alberta Innovates Summer Studentship Award
Oral Presentation at the 2022 Snyder Summer Undergraduate Research Symposium (First Place Winner), the Biomedical Engineering Undergraduate Research Program Symposium, and 4th Annual Canadian Arthritis Research Conference
Poster Presentation at the 2022 McCaig Summer Student Symposium
Poster Tour Presentation at the 2023 Canadian Rheumatology Association Meeting
Upcoming Oral Presentation at the 2023 American College of Rheumatology Meeting

2021-Present **Dr. Eugene Krustev,** Fifth-year rheumatology fellow at the University of Calgary
Dr. Krustev is planning to become a leading myositis expert in Calgary in the near future. He is going away next year after he graduates from the rheumatology program in Calgary to complete a two-year myositis fellowship at John Hopkins with Dr. Lisa Christopher-Stine. Dr. Krustev has been instrumental in helping our team generate ideas and put together three grant proposals for new myositis-related research projects including the 2023 Peter Lougheed Grant, Canadian Institutes of Health Research, and Arthritis Society Career Development Award. An abstract on myositis will be submitted to the 2024 Canadian Rheumatology Association and 2023 Global Conference on Myositis is in progress.

Publications

1. Choi MY, Satoh M, Fritzler MJ. Update on autoantibodies and related biomarkers in autoimmune inflammatory myopathies. Curr Opin Rheumatol. 2023 Jul 28. doi: 10.1097/BOR.0000000000000957. Epub ahead of print. PMID: 37503636. This paper was not directly related to the SOAR project, however, it was written this year to summarize the known and novel autoantibodies for myositis. This provided the background and set the stage for future myositis projects that came from SOAR.
2. Wei J, Tarnopolsky M, Hudson M, Mitchell R, Buhler K, Dufour A, de Almeida L, Fortin P, Boilard E, Becker Y, Hatcher E, Zhang M, Fritzler MJ, Choi M. Novel Machine Learning-Based Diagnostic Algorithm for Sporadic Inclusion Body Myositis Utilizing Comprehensive Autoantibody Profiles. In Submission Annals of Rheumatic Diseases.
3. Wei J, Tarnopolsky T, Hudson M, Mitchell R, Dufour A, Almeida L, Fortin P, Boilard E, Becker Y, Buhler K, Hatcher E, Zhang M, Fritzler M, Choi MY. Machine Learning Analysis

of Sporadic Inclusion Body Myositis Biomarkers [abstract]. The Journal of Rheumatology July 2023, 50 (7 Suppl 1) 7-100; DOI: https://doi.org/10.3899/jrheum.2023-0216

Funding

1. **Granting Agency: University of Calgary**
   Project Title: "SOAR UP: Sporadic Inclusion Body Myositis NOvel Autoantibody and Biomarker Research Utilizing Proteome Microarray"
   Investigators: Choi (PI), Fritzler, Tarnopolsky, Hudson, Costenbader
   Role: Principal Investigator
   6 months, $11,930

2. **Granting Agency: University of Calgary, McCaig Seed Grant**
   Project Title: "Sporadic Inclusion Body Myositis and Proteomic Analysis to Identify Novel Biomarkers (SPIN)"
   Investigators: Choi (Co-PI), Dufour (Co-PI), Fritzler, Mitchell, Tarnopolsky, Hudson, Costenbader
   Role: Co-Principal Investigator
   1 Year, $20,000

3. **Granting Agency: Pfizer**
   Project Title: MDA5 Working Group
   Investigators: Moran-Toro (PI), Choi (Co-I)
   Role: Co-Investigator
   $50,000

4. **Granting Agency: 2023 Peter Lougheed Grant (~$50,000, submitted)**
   Project Title: INSPIRED: INterferon Signature biomarkers for Pulmonary fibrosis in RhEumatic Diseases

5. **Granting Agency: 2023 Canadian Institutes of Health Research (~$750,000, submitted)**
   Project Title: Complement activation Levels and Interferon signature as novel Myositis Biomarkers (CLIMB)

6. **Granting Agency:2023 Arthritis Society Career Development Award (~$375,000, submitted)**

   Project Title: Complement activation Levels and Interferon activity as novel Myositis Biomarkers (CLIMB)

New Projects/Partners:

1. **SOAR UP:** Sporadic Inclusion Body Myositis NOvel Autoantibody and Biomarker Research Utilizing Proteome Microarray, we performed a comprehensive biomarker evaluation in a large cohort of sIBM patients and control comparator sera from patients with other types of myositis, utilizing a complete human proteome microarray (HuProt) as an innovative approach to identify unique autoantibody targets and to apply machine learning methods to interpret a large biomarker dataset. The result of this project was presented at the conferences over the summer by our student Farbod Moghaddam. It will also be submitted as an abstract to the 2023 Global Conference on Myositis.
2. **SPIN:** Sporadic Inclusion Body Myositis and Proteomic Analysis to Identify Novel Biomarkers. We performed a mass spectrometry (MS)-based quantitative shotgun proteomics analysis on sera and muscle biopsy tissue of sIBM patients and control comparators from patients with other types of myositis. The result of this project was presented at the conferences over the summer by our student Farbod Moghaddam. It will also be submitted as an abstract to the 2023 Global Conference on Myositis.
3. **CLIMB:** Complement activation Levels and Interferon signature as novel Myositis Biomarkers study will examine novel biomarkers for the diagnosis, prognosis, and monitoring of myositis. This includes three candidate biomarkers of key mechanisms of inflammation in myositis. To close the seronegative gap, we will combine multiple autoantibody techniques to discover new biomarkers. The results will inform the development and validation of a novel myositis panel. We will validate our findings in a new myositis cohort (n=150) that we will launch in this study. Funding, if successful, will be used to help build the first myositis cohort in Calgary.
4. **INSPIRED:** INterferon Signature biomarkers for Pulmonary fibrosis in RhEumatic Diseases. We will examine novel biomarkers an inflammatory pathway, a key disease pathway for many autoimmune diseases including myositis. I was invited by AstraZeneca to give an international talk about the role of interferon in myositis on October 12, 2023.

5. **MDA5 Working Group:** Several rheumatologists in Calgary have come together to discuss challenging myositis cases led by Dr. Moran-Toro. From this group, we will recruit patients into our myositis cohort.

Collaborators:

1. **Dr. Marie Hudson**, who is a rheumatologist and Associate Professor at McGill University with expertise in myositis. She is the Director of CIMS which will be the main source of clinical data and sera for the myositis patients in this study.
2. **Dr. Mark Tarnopolsky**, a Professor and Division Head of Neuromuscular and Neurometabolic Disorders at McMaster University. He has established expertise and an extensive track record in sIBM research and has built the McMaster sIBM cohort that includes patients from across Ontario.
3. **Dr. Arielle Mendel,** an Assistant Professor, rheumatologist, and early career investigator in autoimmune rheumatic diseases.
4. **Dr. Marvin J. Fritzler**, who is a Professor Emeritus at the University of Calgary and the Director of the MitogenDx Laboratory, a lab focused on developing and commercializing new biomarkers for systemic autoimmune rheumatic diseases.
5. **Dr. Antoine Dufour,** an Associate Professor and Director of the Southern Alberta Mass Spectrometry (SAMS) core facility at the UofC. He will be leading the shotgun proteomics analysis.
6. **Dr. Xavier Bosssuyt**, a Professor of Medicine at the Catholic University of Leuven, Belgium, and a clinical laboratory immunologist. He will be working on CLIMB
7. **Dr. Ross Mitchell (PhD),** a Professor at the University of Alberta and the inaugural Chair in Artificial Intelligence (AI) in Health, and senior program director of AI adoption with Alberta Health Services. He will provide specific expertise in AI/ML
8. **Dr. Stephanie Plamondon** is a physiatrist and leads the Neuromuscular Rehabilitation multidisciplinary clinic at the South Health Campus. She will support the recruitment of new patients into new myositis cohort.
9. **Dr. Cristina Moran-Toro** in a rheumatologist who leads the MDA5 Working Group of rheumatologists who will be recruiting myositis patients.
10. **Yvan St. Pierre** is the statistician on the team who will be working on the biomarker data analysis. He has a Masters in Economics and has worked extensively in the past with Dr. Choi on related projects.

11. **Herb Malcomson** is a Patient Partner who has sIBM and is a member of Myositis Canada. He will provide insight into our study design and conduct knowledge translation activities.
12. **Ms. Katherine Buhler** is our research coordinator and has considerable experience with biomarker data analysis and statistics.
13. **Dr. Carolina De La Rosa** is another research coordinator who will be directly responsible for enrolling patients into the new myositis cohort.
14. **Ms. Jean Kawasoe** is a lab technician in Dr. Choi's laboratory with experience in autoantibody testing and assay development.

We would like to express our heartfelt gratitude to Myositis Canada once again. We hope that our progress to date has met the expectations of the board. Your support and funding have enabled us to make significant discoveries about sIBM, which will assist physicians and researchers in gaining a better understanding of the disease. This, in turn, will lead to earlier and more accurate diagnoses for patients and, ultimately, the discovery of new therapies and a cure. Importantly, your support has been a cornerstone for the establishment of multiple research projects that will position Calgary as a key myositis research center in the future. We have forged critical relationships with collaborators from around the world and have inspired students to pursue careers in medicine, along with further clinical and research training in myositis. We would like to extend our special thanks to Herb Malcolmson for his unwavering support, and we eagerly anticipate continuing to work with him as a Patient Partner.

Yours truly,

May Y. Choi, MD, MPH
Rheumatology Associate Professor, Cumming School of Medicine
HRIC 3A10, 3230 Hospital Drive NW, Calgary, AB T2N 4Z6
Ph: 403-955-8733, Fax: 403-955-8196

Machine Learning Analysis of Sporadic Inclusion Body Myositis Biomarkers

Jenny Wei[1], Mark Tarnopolsky[2], Marie Hudson[3], Ross Mitchell[4], Antoine Dufour[1], Luiz de Almeida[1], Paul Fortin[5,6,7], Eric Boilard[5,6], Yann Becker[6,8], Katherine A. Buhler[1], Erin Hatcher[2], Meifeng Zhang[1], Marvin J. Fritzler[1], May Y. Choi[1]

[1] Cumming School of Medicine, University of Calgary (Calgary,Canada)
[2] Division of Neuromuscular & Neurometabolic Disorders, Departments of Pediatrics and Medicine, McMaster University, Hamilton Health Sciences Centre (Hamilton, Canada)
[3]Department of Medicine, Division of Rheumatology, McGill University, Montreal, Quebec, Canada.
[4]Department of Medicine, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Alberta, Canada.
[5]Faculté de Médecine and Centre de Recherche ARThrite, Université Laval, Québec, QC, Canada.
[6]Centre de Recherche du Centre Hospitalier Universitaire de Québec-Université Laval, Québec, QC, Canada
[7]Division of Rheumatology, CHU de Québec - Université Laval, Québec City, Canada;
[8]Centre de Recherche du Centre Hospitalier Universitaire de Québec-Université Laval, Québec, QC, Canada.

INTRODUCTION

- Sporadic inclusion body myositis (sIBM), a subset of autoimmune inflammatory myopathies (AIM), is often difficult to diagnose (Catalán et al., 2014)
- sIBM does not respond to conventional AIM immunosuppressive therapies, which can be harmful when administered unnecessarily (Needham et al., 2016)
- The objective of this study is to identify novel sIBM biomarkers that would allow for an earlier and more accurate diagnosis and prediction of disease phenotypes using several machine learning (ML) approaches

METHODS

Study Population

- 93 sIBM patients and 137 AIM disease controls
- Patients are from the Tarnopolsky Cohort (McMaster University, Hamilton, ON) and the Canadian Inflammatory Myopathy Study (CIMS)
- Baseline sera of all patients were tested for conventional and novel autoantibodies: ANA, myositis multiplex array (Jo-1, Mi2α, Mi2β, NXP2, TIF1γ, PL7, PL12, PM75, PM100, Ku, SRP, EJ, OJ, Ro52/TRIM21, VCP) and autoimmune liver disease multiplexed array

Aim 1: Determine if sIBM can be differentiated from AIM based on autoantibody biomarkers

- Six classification algorithms were tested and validated using k-fold cross validation to reduce bias and model instability (**Table 1**)

Aim 2: Identify sub-types of sIBM by clustering patients based on clinical and biomarker features

- Hierarchical agglomerative clustering was chosen to allow better visualisation of the data

Aim 3: Analyze biomarker profiles of each sIBM clinical cluster to associate biomarkers with clinical phenotypes

- InterpretML's Explainable Boosting Machine was used to predict feature importances
- Shapley Additive Explanations (SHAP) was used to study the effect of each feature

Table 1
Description of six ML classification algorithms known for high accuracy, interpretability and stability that were tested for differentiating sIBM and AIM.

Algorithm	Description	Equation
K-Nearest Neighbours	Pattern recognition by finding K closest datapoints	
Decision Tree	Flow chart structured classification	
Logistic Regression	Predicts a binary outcome by finding dependency between output and input variables	
Support Vector Machine	Generates a hyperplane to separate categories of data	
Artificial Neural Network	Simulates network of neurons allowing complex analyses.	
Extreme Gradient Boosting	Expansion of decision trees where trees are built additively	

RESULTS

230 individuals studied including 93 sIBM patients (38.7% female, mean age 68.3 +/- 9.1 years) (**Table 3**) and 137 AIM comparators (68.24% female, mean age 56.91 +/- 14.33 years) (**Table 2**).

Table 2. Canadian Inflammatory Myopathy Study (CIMS) autoimmune inflammatory myopathies baseline characteristics.

Parameter	Mean/ Percentage	Parameter	Mean/ Percentage
Age	56.91 ± 14.33	Ethnicity	
Female	68.24%	White	60.81%
Disease Duration	3.50 ± 4.69 Years	Black	8.11%
Age of Onset	54.12 ± 14.76	Latin American	4.73%
Smoking		Asian	8.11%
Never	57.43%	Other	2.70%
Previous	37.16%	Diagnosis	
Current	5.41%	Dermatomyositis	37.84%
Dysphagia as first myopathic symptom	4.05%	sIBM	11.49%
CK (U/L)	2547.15	Polymyositis	4.05%
CK <12 times normal	75.00%	Anti-synthetase Syndrome	5.41%
Associated with cancer	10.14%	IMNM	12.84%
Severity of Myositis at Onset[1]	1.80 ± 0.77	Connective Tissue Disease	2.03%
Quad Femoris Strength (right) [2]	4.77 ± 0.65	Overlap Myositis	31.08%
Quad Femoris Strength (Left) [2]	4.75 ±0.67	Other	1.35%
Severity in Past Month[3]	2.67 ± 1.86		
Arthritis	18.25%		
Dysphagia	32.44%		
Dyspnea	25.68%		
Interstitial Lung Disease	43.24%		
Pulmonary Fibrosis (>0.5 Years)	22.30%		
Global Disease Damage[4]	1.94/10 ± 2.21		

[1]1='Mild' 2='Moderate' 3='Severe' 4='Extremely severe'
[2]Grade out of 5 assigned based on muscle testing
[3]0 = 'No Disease Activity', 10= 'Very Severe Disease'
[4]0 = 'Absent', 10 = 'Maximum'
[5]1= Mild, 2 = Moderate, 3 = Severe

Table 3. McMaster University sIBM baseline characteristics.

Parameter	Mean/ Percentage
Female	38.7 %
Median Age (years)	68.3 ± 9.1 SD
Mean CK level (UI/L)	504.4 ± 288.2 SD
Dysphagia	60.0%
Knee Extension Weakness	93.3%
Grip Weakness	93.3%
Quadriceps Atrophy	98.6%
Mean Disease Severity [5]	1.9 +/- 0.6 SD

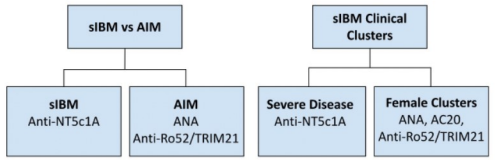

Figure 1. Summary of important biomarkers.

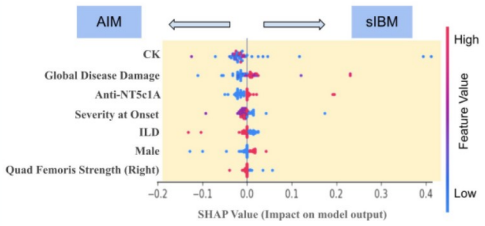

Figure 2. SHAP plot of feature contributions to XGBoost classification of sIBM or AIM. Red points indicate higher value or positivity of the corresponding feature. Blue points indicate lower value or negativity of the feature. The XGBoosting algorithm achieved the highest accuracy at 93.3% for differentiating sIBM from other AIMs based on biomarkers and clinical data

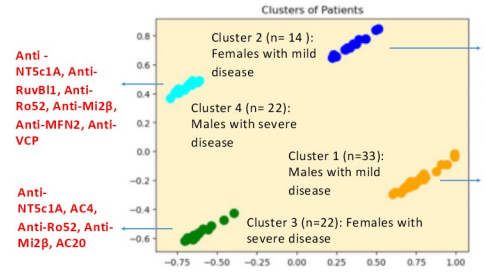

Figure 3. Hierarchical clustering of patients based on clinical phenotypes. Biomarker associations were determined using InterpretML's explainable boosting machine. Axes are based on dimension reduction.

DISCUSSION

AIM 1: sIBM could be differentiated from AIM using ML and biomarkers with high accuracy (93% with extreme gradient boosting)

- The presence of anti-NT5c1A antibodies, negative ANA, and absence of anti-Ro52/TRIM21 were the most helpful predictors

Aim 2 & 3 : Four sIBM clusters differing by sex and disease severity were identified and were associated with different autoantibody profiles

- Anti-NT5C1A was associated with clusters of severe disease phenotype
- Female clusters were associated with positive ANA, particularly the AC20 pattern, and anti-Ro52/TRIM21

CONCLUSIONS

- In this comprehensive ML analysis of established and novel autoantibodies, sIBM could be differentiated from other types of AIM with high accuracy (up to 93%) and can be further classified into four distinct clusters characterized by different sex and disease severity.
- The findings suggest that this may be an important approach to an earlier and accurate diagnosis and prognosis of sIBM to inform treatment decisions
- Future studies to validate our findings in larger cohorts are needed

REFERENCES

[1] Catalán et al., 2014. Autoimmunity Reviews, *13*(4-5), pp. 363.
[2] Needham et al., 2016 Neurotherapeutics, *13(1), pp.*132

ACKNOWLEDGEMENTS

We would like to recognize the sIBM and AIM patients who were involved in this study and funding from Myositis Canada, the University of Calgary VPR Catalyst Fund, the McCaig Institute for Bone and Joint Health, and assay development and performance by MitogenDx. Jenny Wei received funding from the Alberta Innovates Summer Research Studentship and the Arthur J.E Child Chair in Rheumatology Research for this project.

CONTACT

Jenny Wei
University of Calgary
Email: jingyi.wei@ucalgary.ca

Sporadic Inclusion Body Myositis Novel Autoantibody and Biomarker Research Utilizing Proteome Microarray and Mass Spectrometry Proteomics Analysis

Farbod Moghaddam[1], Mark Tarnopolsky[2], Marie Hudson[3], Ross Mitchell[4], Katherine A. Buhler[1], Antoine Dufour[5], Luiz de Almeida[5], Paul Fortin[6,7,8], Eric Boilard[6,7], Yann Becker[7,9], Erin Hatcher[2], Meifeng Zhang[1], Marvin J. Fritzler[1], May Y. Choi[1]

: [1]Division of Rheumatology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada [2]Division of Neuromuscular & Neurometabolic Disorders, Departments of Pediatrics and Medicine, McMaster University, Hamilton Health Sciences Centre (Hamilton, Canada) [3]Department of Medicine, Division of Rheumatology, McGill University, Montreal, Quebec, Canada. [4]Department of Medicine, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Alberta, Canada. [5]Division of Biochemistry and Molecular Biology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada [6]Faculté de Médecine and Centre de Recherche ARThrite, Université Laval, Québec, QC, Canada. [7]Centre de Recherche du Centre Hospitalier Universitaire de Québec-Université Laval, Québec, QC, Canada [8]Division of Rheumatology, CHU de Québec - Université Laval, Québec City, Canada; [9]Centre de Recherche du Centre Hospitalier Universitaire de Québec-Université Laval, Québec, QC, Canada.

Background

- Sporadic inclusion body myositis (sIBM) is a chronic autoimmune disease that associated with severe muscle weakness.
- It is often challenging to diagnose because many patients have no detectable biomarkers (seronegative).
- The pathogenesis of sIBM is not well understood and there are few effective therapies.

Aim

Identify novel biomarkers that can differentiate between sIBM and healthy patients, and examine the potential roles of these novel biomarkers in the pathways of sIBM pathogenesis.

Methods

HuProt

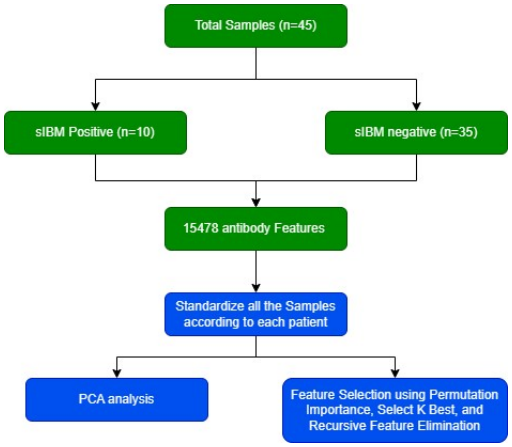

Figure 1. A. HuProt Analysis Approach. A novel approach that is used to identify 20,000 unique **antibody** targets, making up 80% of the human proteome. It works by printing all the proteins on a slide and measuring their interactions with antibodies.

Mass Spectrometry Proteomics

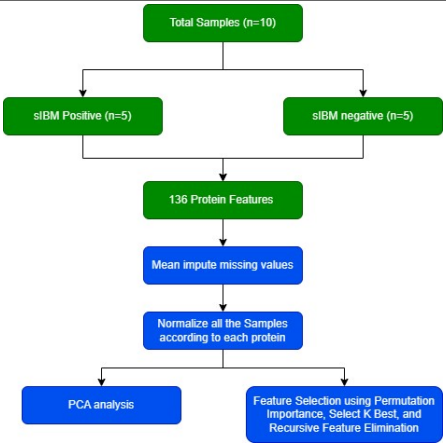

Figure 1. B. Proteomics Analysis Approach. Mass spectrometry proteomics is used to measure **protiens** by breaking down the peptides and separating them using enzymes and liquid chromatography, and then measuring their mass-to-charge ratio using a mass spectrometer. Thousands of protiens can be screened, but for this project proteins with more than 20% missing data were dropped. Remaining 136 proteins were mean imputed

Biomarker Selection

Two different biomarker selection methods were used. The top 10 most important biomarkers selected by each approach were analyzed.

1. **Traditional log-fold change:** log of the difference between the means of the disease and control samples was calculated, as well as the p-values using the students T test. P-values are adjusted according to Benjamini/Hochberg false discovery rate.
2. **Machine learning feature selection:** The three algorithms used were permutation importance, select K best, recessive feature elimination, and the results of these algorithms were combined to generate the final result.

Results

Principle Component Analysis (PCA)

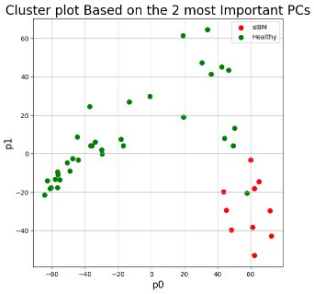

Figure 2A. The two most significant principal components for the HuProt dataset. The red dots are sIBM positive patients while the green dots are the sIBM negative patients

Figure 2B. The two most significant principal components for the proteomics dataset. The red dots are sIBM positive patients while the green dots are the sIBM negative patients

Top 10 Antibody and Proteins Selected

HuProt Antibodies directed to:		Mass-Spectrometry Proteins	
Machine Learning	Log-Fold Change	Machine Learning	Log-Fold Change
SNX33	RABGAP1L	FBLN1	FBLN1
RABGAP1L	MPRIP	C4A	ITIH3
EIF3L	SNX33	FGA	VWF
VDAC1	RAD52	ITIH3	C4A
GNB5	HPGD	C1QC	FGA
OPHN1	FYTTD1	IGLL5	C1QC
PLB1	SLC35A3	VWF	IGLL5
SDS	SNX12	IGHV5-51	IGHV5-51
IGHG3	HPD	IGHV1-18	C5
DIXDC1	ZFP41	NCAPD3	TTR

Antibodies/proteins that were identified by both machine learning and log-fold change methods are highlighted in the same color.

Conclusion

This study discovered several potential novel diagnostics and pathogenic sIBM biomarkers. Further studies are underway to test whether these antibodies and proteins can be detected in the muscle and validated in a larger cohort of sIBM patients.

Among these biomarkers, most could be involved in the putative degenerative and inflammatory pathways of sIBM pathogenesis:

- **Abnormal cytoskeletal organization (anti-SNX33)**
- **Complement system activation (C4A, CIQC)**
- **Autoantibody production (IGLL5, IGHV5-51)**

Funded by McCaig Institute for Bone and Joint Health Seed Grant