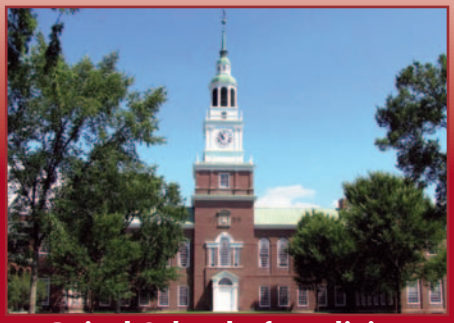
NIAMS NATIONAL SCLERODERMA Core Centers

Boston University



Geisel School of Medicine at Dartmouth

Northwestern University

Medical University of South Carolina

www.bu.edu/SScores

Boston University School of Medicine
Scleroderma Research Center

Overview

The Boston University Scleroderma Core Centers (or SScores) provides a framework for more rapid advances in understanding systemic sclerosis (SSc) pathogenesis by providing pathologic skin and lung samples, and advanced technologies, microarray gene expression and proteomics, to existing and new SSc investigators.

The Core Centers coordinate robust clinical data collection to empower pathological tissue analyses and application of advanced technologies, providing uniform clinical assessments, high level analytical capabilities and large sample numbers.

Thus, the Core Centers accelerate research into SSc pathogenesis by helping individual investigators in their research projects, fostering collaboration between investigators through utilization of core resources, and creating consortia data that will empower further clinical-translational insights.

What can the SScores do for me and my research?

Basic Interaction

- I need the Core to embed, cut and stain some skin tissues for me
- No samples from the Core
- No clinical information
- Core provides: access to below market cost services. No collaborative agreement is needed

Intermediate Core Interaction

(I want to know if the gene/protein I study is important in scleroderma pathogenesis)

- Obtain scleroderma and control skin samples for analysis of your target protein from the DermPath Core, correlate with clinical data or
- Obtain lung pathology samples for analysis of your protein from the Lung Histopathology Core, correlate with clinical data or
- Obtain sera from the Proteomic Core for measuring expression of your protein, correlate with clinical data

Complete Interaction

- I am going to submit skin and/or blood samples to the Cores
- I am going to submit associated clinical information
- I am going to use this as a vehicle to accelerate my discoveries in scleroderma
- I am going to anticipate consortia authorship on group publications ranging from proteomics, immunohistochemistry to clinical database analyses

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The Dermatopathology Core
at Boston University

PI – Jag Bhawan, MD

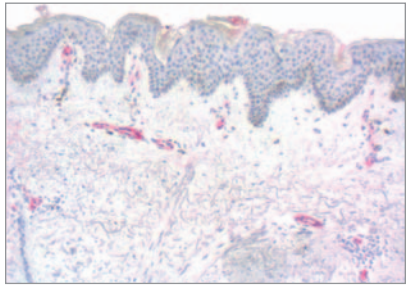
Contact – Salma Goummih, 617.638.5569, sgoummih@bu.edu

Dermatopathology Fee Schedule*

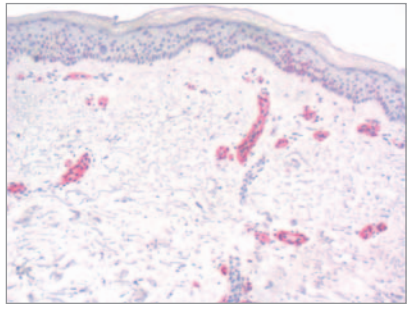
	Embedding formalin-fixed skin	Sectioning paraffin block	H&E Stain	IHC Stain
Human sample associated with MRSS/clinical data; sample remainder donated to core for future use.	No cost	Up to 5 unstained slides at no cost	Up to 1 at no cost	Up to 1 at no cost
Human sample not associated with MRSS/clinical data; not being donated for future use.	$5.00/sample	$2.00/slide	$2.00/slide	$15.00/slide
Mouse sample	$5.00/sample	$2.00/slide	$2.00/slide	$15.00/slide

** Prices subject to change*

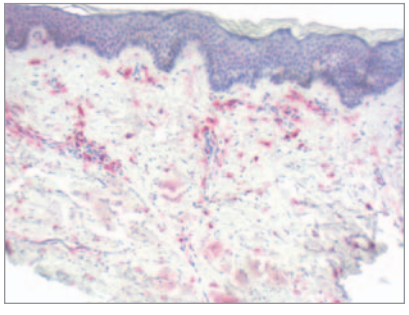
Von Willebrand Factor



Smooth Muscle Actin



CD163



Antibodies Currently Available for Immunohistochemical (IHC) Staining

Antibody	Clone	Manufacturer
Smooth Muscle Actin	1A4	Dako
Von Willebrand Factor	F8/86	Dako
CD163	10D6	Novocastra
P300	C-20	Santa Cruz Biotechnology

We can also work with any other antibodies not listed to develop staining protocols.

This Core will provide uniform processing of skin samples from various investigators. We have a well-established method of preparing 8 skin samples in one block to save costs as well as avoid variability of staining between samples. We have state-of-the-art automated equipment for routine histopathology and immunopathology needs. The lab is equipped with a photomicroscope with a digital camera which can make excellent photomicrographs. Our image analysis system can evaluate various parameters in an objective manner.

In addition to routine histopathology, immunostaining with any antibody can be performed. The director has tremendous experience with various antibodies including SMA, CD31, lymphocyte markers, CD34, and cathepsin k, most relevant to this field.

The Lung Pathology Core
at The Medical University of South Carolina

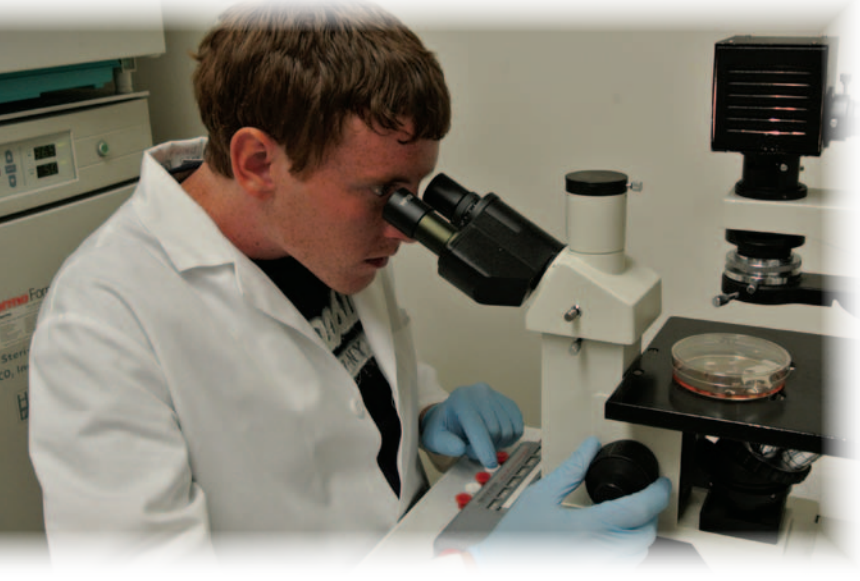
PI – Carol Feghali-Bostwick, PhD

Contact – Carol Feghali-Bostwick, 843.792.3484, feghalib@musc.edu

The Lung Pathology Core will

- Generate medium and high-density tissue microarrays (TMA) using lung tissues of patients with SSc-PF, SSc-PAH, the idiopathic forms of the disease, and normal donors as a resource for the SSc Core Center investigators. These unique tissue samples can then be stained all at one time
- Provide comprehensive clinical information on patients from whom lung tissues are obtained, facilitating correlation studies of tissue microarray analysis and disease clinical variables
- Provide a TMA service for investigators conducting their own animal research who will provide lung tissues for the generation of tissue arrays. Sections from the array blocks will be provided for use in immunohistochemistry, in situ hybridization, or other assays

Additional details and fees are available at
http://www.bu.edu/SScores/



Lung Tissue Array Fees

Construction of Block

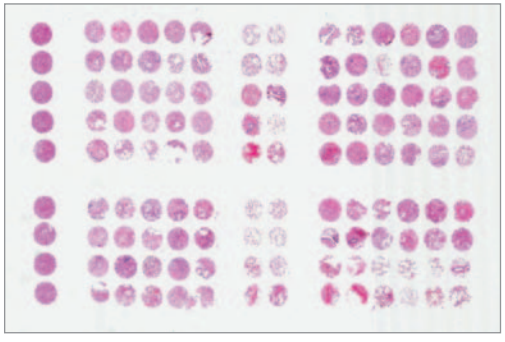
The construction of the TMA block is broken down into classes that reflect the number of cores requested per block. The cost for each class is as follows:*

Class	Number of Cores/Blocks	Charge
	Up to 10	$150
I	Up to 25	$800
II	Up to 50	$1250
III	51 to 100	$1550
IV	100 to 150	$1750
V	150 to 200	$2000
VI	200 to 250	$2250
VII	250 to 300	$2500

Additional Fees:

1. **H&E sections of parent block ($10/slide)**
   All paraffin blocks must be recut to map most recent surface of block detail before blocks can be cored.
2. **Design Set Up ($250)**
   This is a one time charge for any new array construction. The requesting investigator has input in the design process and receives a copy of the template for final approval.
3. **Pathologist Service ($15/sample)**
   This charge will apply if a pathologist is needed to evaluate the H&E and circle the area of interest that will be cored.
4. **Sectioning of TMA**
   Sectioning of TMA block by Tape transfer for blank slides. A different fee is designated for blocks generated for the SI vs requests for sections of pre-existing TMA.
5. **H&E stain of TMA slide ($15/slide)**
   Staining of Tape TMA blank slides.

** Prices subject to change*



Tissue microarray of lung tissue from patients with scleroderma, IPF, and normal donors

The Proteomics Core
at Northwestern University

PI – John Varga, MD; Co-PI – Monique Hinchcliff, MD, MS

Contact – Mary Carns, 312.503.1137, m-carns@northwestern.edu

Description: The Proteomics Core provides the technology for analyzing hundreds of proteins in the blood. By offering high quality multiplexed assay analyses, we aim to facilitate the discovery of important protein classification and risk stratification related to scleroderma. These analyses may lead to insights into the pathogenesis, progression, and response to treatment of scleroderma.

Benefit to You: Investigators will have access to state-of-the-art commercially available analysis tools at a 50%-75% reduced cost. Additionally, associations with clinical data entered into the Clinical Core will be facilitated.

Procedure: Investigators will submit a small volume of sera to the Proteomics Core. The Core will batch, barcode, and send the samples for analysis. Analysis is performed at Myriad-Rules Based Medicine, a biotechnology company specializing in proprietary protein-based products and services across the life sciences spectrum. Samples will be run on the DiscoveryMAP® v1.0 or DiscoveryMAP® 250+ v.1.0, which include over 100 and 250 analytes respectively, measuring markers of infectious disease, autoimmunity, cardiovascular risk, cancer, hormones, cytokines/chemokines, acute phase reactants, clotting proteins, growth factors, tissue modeling factors, and other analytes with currently unknown function. To reduce costs and enhance the clinical utility of proteomic analysis, we will develop an SSc biomarker panel. The panel will then be validated in a discovery cohort. Once available, this panel will examine a core set of ~20 analytes that show statistical significance compared to controls. Bioinformatics analyses of proteomic data and corresponding data in the Clinical and Microarray Cores will also be available.

Myriad RBM DiscoveryMAP® 250+ v. 1.0

1. 6Ckine
2. Adiponectin
3. AgRP
4. Aldose Reductase
5. Alpha-1 Antichymotrypsin
6. Alpha-1 Antitrypsin
7. Alpha-1 Microglobulin
8. Alpha-2 Macroglobulin
9. Alpha Fetoprotein
10. Amphiregulin
11. Angiogenin
12. Angiopoietin-2
13. Angiotensin-Converting Enzyme
14. Angiotensinogen
15. Apolipoprotein A-I
16. Apolipoprotein A-II
17. Apolipoprotein A-IV
18. Apolipoprotein B
19. Apolipoprotein C-I
20. Apolipoprotein C-III
21. Apolipoprotein D
22. Apolipoprotein E
23. Apolipoprotein H
24. Apolipoprotein (a)
25. AXL Receptor Tyrosine Kinase
26. B cell-activating Factor
27. B Lymphocyte Chemoattractant
28. Beta-2 Microglobulin
29. Betacellulin
30. BMP-6
31. BDNF
32. Calbindin
33. Calcitonin
34. Cancer Antigen 125
35. Cancer Antigen 15-3
36. Cancer Antigen 19-9
37. Cancer Antigen 72-4
38. CEA
39. Cathepsin D
40. CD 40 antigen
41. CD 40 Ligand
42. CD 5 antigen-like
43. Cellular Fibronectin
44. Chemokine CC-4
45. Chromogranin A
46. Ciliary Neurotrophic Factor
47. Clusternin (Apo J)
48. Collagen, IV
49. Complement C3
50. Complement Factor H
51. Connective Tissue Growth Factor
52. Cortisol
53. C-Peptide
54. C Reactive Protein
55. Creatinine Kinase-MB
56. Cystatin C
57. Endoglin
58. Endostatin
59. Endothelin-1
60. ENRAGE
61. Eotaxin -1
62. Eotaxin -2
63. Eotaxin -3
64. Epidermal Growth Factor
65. Epidermal Growth Factor Receptor
66. Epiregulin
67. EpCAM
68. ENA-78
69. Erythropoietin
70. E-selectin
71. Ezrin
72. Factor VII
73. FAS Ligand
74. FASLG Receptor
75. FABP adipocyte
76. FABP heart
77. FABP liver
78. Ferritin
79. Fetuin A
80. Fibrinogen
81. FGF-4
82. FGF basic
83. Fibulin-1C
84. Follicle Stimulating Hormone
85. Galectin-3
86. Gelsolin
87. Glucagon
88. GLP-1 total
89. Glucose 6 Phosphate Isomerase
90. GCLR subunit
91. GST alpha
92. GST Mu1
93. G-CSF
94. GM-CSF
95. Growth Hormone
96. Growth-Regulated alpha protein
97. Haptoglobin
98. HE 4
99. Heat Shock Protein 60
100. HB-EGF Like Growth Factor
101. Hepatocyte Growth Factor
102. Hepatocyte Growth Factor Receptor
103. Hepsin
104. HCG beta
105. HEGFR 2
106. Immunoglobulin A
107. Immunoglobulin E
108. Immunoglobulin M
109. Insulin
110. IGFBP-1
111. IGFBP-2
112. IGFBP-3
113. IGFBP-4
114. IGFBP-5
115. IGFBP-6
116. ICAM-1
117. Interferon gamma
118. Interferon gamma Induced Protein10
119. Interferon-inducable T-cell alpha chemoattractant
120. IL-1 alpha
121. IL-1 beta
122. IL-1 receptor antagonist
123. Interleukin 2
124. IL-2 Receptor alpha
125. Interleukin 3
126. Interleukin 4
127. Interleukin 5
128. Interleukin 6
129. Interleukin 6 Receptor
130. Interleukin 6 Receptor subunit beta
131. Interleukin 7
132. Interleukin 8
133. Interleukin 10
134. Interleukin 12 Subunit p 40
135. Interleukin 12 Subunit p 70
136. Interleukin 13
137. Interleukin 15
138. Interleukin 16
139. Interleukin 25
140. Kallikrein -5
141. Kallikrein -7
142. Kidney Injury Molecule-1
143. Lactoylglutathione lyase
144. LAP TGF-b1
145. Lectin-like Oxidized LDL Receptor 1
146. Leptin
147. Luteinizing Hormone (LH)
148. Lymphotactin
149. MC-S Factor 1
150. MIP-1 alpha
151. MIP-1 beta
152. MIP-3 alpha
153. MIP-3 beta
154. MMIF
155. Macrophage-Derived Chemokine
156. Macrophage Stimulating Protein
157. MM LDL
158. Maspin
159. MMP-1
160. MMP-2
161. MMP-3
162. MMP-7
163. MMP-9
164. MMP-9, total
165. MMP-10
166. Mesothelin
167. MHC class I chain-related A
168. MCP-1
169. MCP-2
170. MCP-3
171. MCP-4
172. MIG Interferon
173. MPIF-1
174. Myeloperoxidase
175. Myoglobin
176. NGF-beta
177. NrCAM
178. Neuron Specific Enolase
179. Neuropilin-1
180. NGAL
181. NT-proBNP
182. Nucleoside diphosphate kinase B
183. Osteopontin
184. Osteoprotegrin
185. Pancreatic Polypeptide
186. Pepsinogen I
187. Peptide YY
188. Peroxiredoxin 4
189. Phosphoserine Aminotransferase
190. Placental Growth Factor
191. PAI-1
192. PDGF-BB
193. PAPP A
194. Progesterone
195. Proinsulin, intact
196. Proinsulin, total
197. Prolactin
198. Prostasin
199. PSA, free
200. PAP
201. Protein S100-A4
202. Protein S100-A6
203. PARC
204. RAGEP
205. ErbB-3
206. Resistin
207. S100 b
208. Secretin
209. Serotransferrin
210. Serum Amyloid P
211. SGOT
212. SHBG
213. Sortilin
214. SCCA-1
215. Stem Cell Factor
216. Stromal cell-derived Factor 1
217. SOD 1
218. T Lymphocyte-Secreted Protein I-309
219. Tamm-Horsfall Urinary Glycoprotein
220. T-Cell Specific Protein RANTES
221. Tenascin C
222. Testosterone, Total
223. Tetranectin
224. Thrombomodulin
225. Thrombopoietin
226. Thrombospondin-1
227. Thyroglobulin
228. Thyroid Stimulating Hormone
229. Thyroxine-Binding Globulin
230. Tissue Factor
231. TIMP-1
232. tPA
233. TRAIL-R3
234. TGF alpha
235. TGF beta-3
236. Transthyretin
237. Trefoil Factor 3
238. TNF-alpha
239. TNF-beta
240. TNF-RI
241. TNF-RII
242. Tyrosine kinase Ig EGF
243. uPA
244. uPAR
245. VCAM-1
246. VEGF
247. VEGF-B
248. VEGF-C
249. VEGF-D
250. VEGF-R1
251. VEGF-R2
252. VEGF-R3
253. Vitamin K-dependent S
254. Vitronectin
255. vWF
256. YKL-40

www.bu.edu/SScores

The Microarray Core
at Geisel School of Medicine at Dartmouth

PI – Michael Whitfield, PhD

Contact – Tammara Wood, 603.650.1105, tammara.a.wood@dartmouth.edu

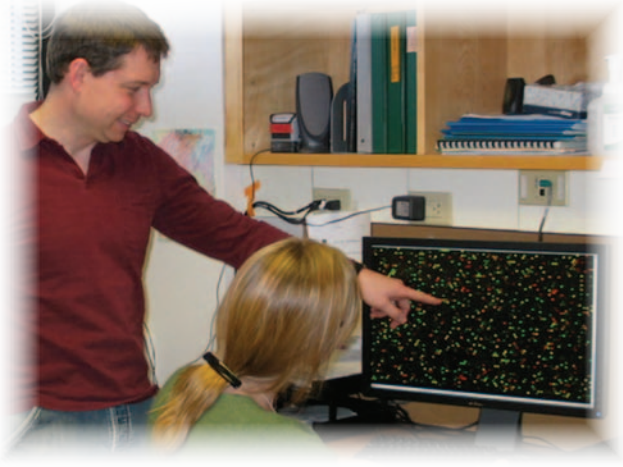
The Core will provide:

- Experimental design consults
- Digital barcoding and sample tracking
- Automated high quality RNA production
- Quality control using standardized and proven protocols
- Samples hybridized to Agilent whole-genome DNA microarrays
- RNA-seq Whole Transcriptome Shotgun Sequencing
- Basic dataset analysis

Additional bioinformatic analyses can be performed (call for pricing).

The Core website has a detailed RNA quality guide as well as a Sample Collection Protocol insuring sufficient RNA for analysis.

Visit: www.bu.edu/SScores/ for more details.



Clinical Data Collection
at Boston University

Through **Boston University's Data Coordinating Center**, we will carefully collect and characterize primary and secondary clinical outcomes and provide this information to the investigators in individual projects and work closely with these investigators and the Proteomic and Microarray Cores in cross-sectional and longitudinal analyses of gene and protein expression patterns and their relationship to changes in clinical disease features. The clinical data arm of the National Scleroderma Core Centers will function to carefully characterize a cohort of subjects with SSc (drawn from a large referral center) followed prospectively to link their clinical data, disease progression and severity with biologic mechanistic data.

Authorship Guidelines

Core Directors or other Core personnel will, in some but not all cases, reasonably anticipate co-authorship on publications arising from core activities. The defining line for this will not be any different from collaborations that might occur outside the core structure. To avoid misunderstandings authorship questions will be defined at the time core service are initiated.

In addition to Core Director authorship rights, Core Investigator/Users will also have rights as co-authors based on sample and or clinical database contributions to cores. For example, one of the more exciting anticipated outcomes of core utilization will be the generation of large datasets that include many or even all of the consortia of investigators. Core investigators/Users can reasonably expect to be included as authors for publications that include data from submitted samples and associated clinical data.

An example serves to illustrate this most easily. The dataset generated from all the investigators utilizing the Proteomic Core will likely provide a powerful database for understanding the relationships between circulating cytokine levels and clinical features. Publications resulting from these analyses will include all Core Investigators submitting samples unless an investigator explicitly and in writing wishes to be excluded from authorship.

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