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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
The Dermatopathology Core at Boston University

PI – Jag Bhawan, MD
Contact – Salma Goummih, 617.638.5569, sgoummih@bu.edu

Dermatopathology Fee Schedule*

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

* Prices subject to change

Antibodies Currently Available for Immunohistochemical (IHC) Staining

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Clone</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth Muscle Actin</td>
<td>1A4</td>
<td>Dako</td>
</tr>
<tr>
<td>Von Willebrand Factor</td>
<td>F8/86</td>
<td>Dako</td>
</tr>
<tr>
<td>CD163</td>
<td>10D6</td>
<td>Novocastra</td>
</tr>
<tr>
<td>P300</td>
<td>C-20</td>
<td>Santa Cruz Biotechnology</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>Class</th>
<th>Number of Cores/Blocks</th>
<th>Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Up to 10</td>
<td>$150</td>
</tr>
<tr>
<td>II</td>
<td>Up to 25</td>
<td>$800</td>
</tr>
<tr>
<td>III</td>
<td>Up to 50</td>
<td>$1250</td>
</tr>
<tr>
<td>IV</td>
<td>51 to 100</td>
<td>$1550</td>
</tr>
<tr>
<td>V</td>
<td>100 to 150</td>
<td>$1750</td>
</tr>
<tr>
<td>VI</td>
<td>150 to 200</td>
<td>$2000</td>
</tr>
<tr>
<td>VII</td>
<td>200 to 250</td>
<td>$2250</td>
</tr>
<tr>
<td>VIII</td>
<td>250 to 300</td>
<td>$2500</td>
</tr>
</tbody>
</table>

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
The Proteomics Core

at Northwestern University

Pl – John Varga, MD; Co-Pl – 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+ v1.0, 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.
The Genomics & Bioinformatics 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
• Sample tracking
• Automated high quality RNA extraction
• RNA quality control using validated, standardized protocols
• Agilent whole-genome DNA microarray hybridization for human and mouse gene expression
• RNA-Seq Transcriptome Sequencing
• NanoString analysis of mRNA, miRNA, custom mRNA-miRNA panels
• Basic data analysis

Additional bioinformatic analyses available; please call for pricing.
The Core website has a detailed RNA quality guide as well as a Sample Collection Protocol insuring acceptable 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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