National Mesothelioma Virtual Tissue Bank (NMVB) (http://www.mesotissue.org) 
Supported by CDC/NIOSH Grant U24OH009077-07

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Nancy Whelan  Project Manager
Waqas Amin  Research Associate

Participants (confirmed):
Adele M. Childress (CDC)  Ainsley Weston (NIOSH)
Harvey Pass (NYU)  Raja Flores (MSSM)
Jonathan Melamed (NYU)  Michael Feldman (U Penn)
Arjun Pennathur (U Pitt)  Anil Vachani (U Penn)
James Pingpank (U Pitt)  James Luketich (U Pitt)
David Bartlett (U Pitt)  Mary Hesdorffer (Meso Fndn)
Rodney Landreneau , MD (U Pitt)

CDC  NIOSH  NYU  MSSM  Penn  Meso Fndn
Overview:

- The National Mesothelioma Virtual Bank (NMVB) provides de-identified annotated mesothelioma biospecimens to the mesothelioma research community.

- The NMVB database allows a user to query the biospecimen resource to identify cohorts for translational research.

- We collect retrospective and prospective mesothelioma cases at four major sites Mount Sinai School of Medicine (MSSM), New York University (NYU), University of Pennsylvania (U Penn) and University of Pittsburgh (U Pitt).

- Key to this resource is continued annotation of mesothelioma biospecimens including demographic, epidemiologic, clinicopathologic, follow-up and recurrence data for all biospecimens collected.

- We then provide well-annotated high quality mesothelioma biospecimens and data to approved researchers via a Letter of Intent – see http://www.mesotissue.org/apply.cfm
Achievements:

- New Collaborator: Mount Sinai School of Medicine (MSSM) is brought on board to expand the specimen collection to meet the research requirements in 2011 competitive renewal.

- Collaborated as Pathology Informatics Core in NCI Mesothelioma SPORE Grant.

- Three tissue microarrays have been developed and are available for investigators at NYU, U Penn and U Pitt which are now the 2nd most requested biospecimen type.

- 21 Specimens Requests are completed (which doesn’t include 3 TCGA requests)

- Marketing efforts are expanded to provide information regarding the resource to a larger community of researchers via mass marketing e-mails, publications and national/international conferences.
NMVB Resource Organization:

STEERING COMMITTEE
Member are Principle/Co-Investigator of NMVB & CDC/NIOSH

RESEARCH EVALUATION PANEL (REP)

MESO-FOUNDATION:
Mesothelioma Advocacy Group

WORKING GROUP:
Members are data managers, Tissue Bank Technicians, Cancer Registrars and Clinical Nurse Coordinators

NMVB-CENTRAL DATA MANAGEMENT CORE

NYU
U. Penn
UPMC
MSSM
Mesothelioma Consenting, Tissue Banking and Clinical Data annotation workflow

TBIS: Tissue Bank inventory System,
RIS: Registry Information System,
CTTK: Clinical Trial Tool Kit,
NMVB: National Mesothelioma Virtual Bank
Specimen Collection:

Tissue bank protocols are followed in the collection and storage by tissue bank technicians.

Specimen Types:

- Tissue Microarray with Clinical Data Annotation
- Fresh Frozen Tissues
- Blood Products: Serum, RBC, Plasma, Whole blood, Buffy Coat, etc...
- Paraffin embedded blocks
Nurse coordinator notifies Health Sciences Tissue Bank (HSTB) personnel prior to the patient’s surgery of NMVB tissue candidate and follows up by faxing a consent to the HSTB.

E-mail notification to Post Doc and Project Coordinator on the upcoming surgery.

Surgical tissue is picked up at the OR and brought to the Gross Dissection room and is triaged under the auspices of a Pathologists’ Assistant.

The Surgical tissue is assigned a NMVB Study number.

Each portion received from the Pathologists’ Assistant (determined by amount and size of tissue) is to be divided into three portions:

- Bulk Frozen
- Formalin Tissue
- Fresh frozen OCT

Bulk frozen is kept in bitran bag and stored in -80°C.

Taken to research histology lab for processing to formalin fixed paraffin embedded (FFPE).

FF OCT is stored in a heat sealed bag @ -80°C.
Nuncs should be labeled and aliquot as shown below and record on specimen sheet:
- 2 WB (whole blood – purple top before spinning)
- 2 B (buffy coat)
- 2 R (red blood cells)
- 10-20 P (plasma)
- 10-20 S (serum)

Research nurse coordinator call the tissue bank when patient is consented and pre-op, operative and post-op blood samples are drawn.

Blood is tubed to Gross Dissection Room in the Department of Pathology.

Tissue bank tech. receives 2-3 small purple tops and 1-2 large red tops along with a consent for the patient.

Nunc vials for the separated blood products are labeled with the NMVB Study# by tissue bank technician.

Before the purple tops are centrifuged, aliquot 2 nuncs with whole red blood. All peripheral blood tubes are put through the centrifugation process.

Purple top yields plasma, buffy coat and red blood cell aliquots.

Red top yields serum aliquots.
Data Management:

- Coordinating site (UPMC) ensures implementation of policies and guidelines directed by Steering Committee.
- Implements and monitors patient’s consenting/ enrollment, data and specimen collection protocols at coordinating and collaborative site.
- Perform quality assurance and control of data twice in year to ensure high quality of annotations.
- Monitor and regulate request specimen fulfillment protocol.
Letter of Intent (LOI) Status Report:

Total Number of Requests: 23

- Approved LOI 21
- Completed 21
- Specimens Request In Process: 1
- LOI request on Hold: 0
- Rejected/Closed 2

Average turnaround from initial request to getting specimens is about 6 weeks.
NMVB Total Accruals:

- Total Number of Patients Participating: 1075
- Total # Specimen/Patient Instances: 1343
- Total Number of Tissue Samples: 1015
## Total Accrual Analysis/Year (Cumulative):

<table>
<thead>
<tr>
<th>Year</th>
<th>Retrospective Cases</th>
<th>Prospective Cases</th>
<th>Overall NMVB Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>515</td>
<td>8</td>
<td>523</td>
</tr>
<tr>
<td>2007</td>
<td>574</td>
<td>61</td>
<td>635</td>
</tr>
<tr>
<td>2008</td>
<td>594</td>
<td>116</td>
<td>710</td>
</tr>
<tr>
<td>2009</td>
<td>663</td>
<td>173</td>
<td>836</td>
</tr>
<tr>
<td>2010</td>
<td>668</td>
<td>235</td>
<td>903</td>
</tr>
<tr>
<td>2011</td>
<td>679</td>
<td>305</td>
<td>984</td>
</tr>
<tr>
<td>2012</td>
<td>692</td>
<td>383</td>
<td>1075</td>
</tr>
</tbody>
</table>
## Percentage of contribution / Each Site:

<table>
<thead>
<tr>
<th>Institutions</th>
<th>Retrospective Cases</th>
<th>Prospective Cases</th>
<th>Overall NMVB Total</th>
<th>% contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYU</td>
<td>157</td>
<td>97</td>
<td>254</td>
<td>24%</td>
</tr>
<tr>
<td>U. Penn</td>
<td>126</td>
<td>126</td>
<td>252</td>
<td>24%</td>
</tr>
<tr>
<td>*MSSM</td>
<td>6</td>
<td>10</td>
<td>16</td>
<td>1%</td>
</tr>
<tr>
<td>UPitt</td>
<td>403</td>
<td>150</td>
<td>553</td>
<td>52%</td>
</tr>
<tr>
<td>Total</td>
<td>692</td>
<td>383</td>
<td>1075</td>
<td>100%</td>
</tr>
</tbody>
</table>

*MSSM Joined the resource in November 2012
**NMVB Accrual-Surgical Specimens:**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Surgical Procedure Type</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Biopsy Specimen</td>
<td>Resected Specimen</td>
<td></td>
</tr>
<tr>
<td>Paraffin</td>
<td>144</td>
<td>298</td>
<td></td>
</tr>
<tr>
<td>Fresh Frozen</td>
<td>39</td>
<td>332</td>
<td></td>
</tr>
<tr>
<td>Bulk Frozen</td>
<td>10</td>
<td>75</td>
<td></td>
</tr>
</tbody>
</table>
NMVB Accrual-Blood Products:

- Whole Blood, 254
- Plasma, 339
- Buffy Coat, 282
- Serum, 337
- Red Blood Cells, 190
- Buffy Coat, 282
NMVB Accrual-Harmful Substance Exposure:

- Asbestos, 438
- Other Exposures, 187
- Unknown, 362
- No Exposure, 88
**NMVB Tissue Microarrays (TMAs):**

- Tissue Microarray (TMA) is used to examine the distribution of marker molecules in hundreds of different tissues displayed on a single slide.

- **U Pitt TMA:** 40 Mesothelioma cases. 36 cases have tissue cores from the primary lesion, 3 patients have tissue cores from a metastatic lesion and 1 patient has tissue cores from both the primary and metastatic lesions.

- **U. Penn TMA:** 4 TMA slides contain 55 mesothelioma cases. The TMA slides hold tissue core of primary, metastatic mesothelioma and control samples.

- **NYU TMA:** 37 cases have been included in the development of TMA which included primary metastatic, mixed lesions and control sample.

- TMA data excel, XML and maps files are available on the web site (www.mesotissue.org)
The Process:

- Melissa Culligan, RN, CCRC for the thoracic surgical team, approaches and consents patients for biospecimen collection. Once the patient consents, Melissa contacts the TTAB technician with the patient’s information.

- On the day-of-surgery, the TTAB technician tracks the progression of the surgical procedure using NaviCare, the hospital’s patient tracking software.

- One hour after incision occurs the technician accesses the OR to collect blood and urine, if available, and returns to the TTAB bench located within Surgical Pathology, which is less than 2 minutes away.

- While processing the fluids at the TTAB bench, the Tech will receive a page that tissue is available for pick-up.
The Collection...

- Typical collection yields 50 cc of blood & 40 cc of urine,...which is then processed into:
  - 10 Plasma CPT aliquots
  - 18 Plasma EDTA aliquots
  - 8 Serum aliquots
  - 5 Packed RBCs
  - 2 PBMC aliquots
  - 3 Whole bloods
  - 4 Buffy coat aliquots
  - 2 Urine aliquots
Histologic confirmation & classification by Dr. Feldman.

Technician enters data in NMVB database.
Prospective Collections:

Dec 2011 through Dec 2012

33 Subjects Collected

- 32 new subjects
- 1 subject with follow up procedures/collections
- 18 Pleurectomies (no other procedure performed)
- 15 Biopsies (no other procedure performed)
Looking back in comparison...

Dec 2011 – Dec 2012

33 Cases

- 18 Pleurectomies
- 15 Biopsies

Dec 2010 – Dec 2011

23 Cases:

- 16 Pleurectomies (3 with associated biopsies)
- 4 Biopsies
Retrospective Collections:


- 6 Retrospective cases have been identified and retrieved from archives.
- These are now available to NMVB as paraffin blocks.
Prospective Specimen Yield, in Total...

**Tissue:**
- 211 Fresh-frozen tumor samples
- 162 OCT blocks of tumor
- 305 Paraffin embedded blocks

**Fluid Biospecimens:**
- 288 Plasma EDTA aliquots
- 160 Plasma CPT aliquots
- 128 Serum aliquots
- 80 Packed RBCs
- 31 PBMC aliquots
- 31 Whole bloods
- 64 Buffy coat aliquots
- 32 Urine aliquots
2012 NYU NMVB Report

NYU Dept of Cardiothoracic Surgery
NYU Dept of Pathology
Tuesday, December 11th, 2012
Personnel at NYU:

Dept. Cardiothoracic Surgery

Harvey Pass, MD
(Surgeon, NYU Steering Committee Member & PI)

Audrey Sorensen, RN
(Research Nurse Coordinator)

Ryan Harrington
(Lab Technician, Thoracic Lab)

Angela Pittman
(Research Project Coordinator)

Dept. Pathology

Jonathan Melamed, MD
(Pathologist, NYU Steering Committee Member)

Ruth Pe Benito
(Bioresource Manager)

Monica Gorman
(Research Coordinator)

Rachel Ruoff
(Lab Technician, Pathology Lab)
### NYU Additions to NMVB 2012:

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>Serum</th>
<th>Plasma</th>
<th>Buffy Coat</th>
<th>Mono</th>
<th>CPT</th>
<th>Tumor</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesothelioma Follow-up (n=5)*</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Mesothelioma New (n=11)*</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>4</td>
</tr>
</tbody>
</table>

*blood products as per cardiothoracic surgery research staff, but have limited availability of data due to Sandy*
### NYU NMVB Biospecimen Accrual:

<table>
<thead>
<tr>
<th>Year</th>
<th>Retrospective Specimens Collected</th>
<th>Prospective Specimens Collected</th>
<th>Overall Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>157</td>
<td>31</td>
<td>188</td>
</tr>
<tr>
<td>2008</td>
<td>0</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>2009</td>
<td>0</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>2010</td>
<td>0</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>2011</td>
<td>0</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>2012</td>
<td>0</td>
<td>16*</td>
<td>16</td>
</tr>
</tbody>
</table>

**Total:** 255

*both new and follow-up case total*
### NYU NMVB Tissue Accrual:

<table>
<thead>
<tr>
<th>Year</th>
<th>New cases collected</th>
<th>Collection Method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Frozen tissue only</td>
</tr>
<tr>
<td>2008</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>2009</td>
<td>9</td>
<td>2</td>
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<tr>
<td>2010</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>2011</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>2012</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>
Quality Assurance for Accrual 2012:

- Conducted PowerPath (pathology database) search for all mesothelioma cases in 2012
- 18 patients with surgeries and confirmed mesothelioma at NYU in total
- 16 of those patients were recruited in 2012 or have been recruited in past for NMVB by Cardiothoracic Department Staff
- Nearly 90% recruitment of NYU mesothelioma patients for 2012
TCGA Project:

- All NYU samples shipped to TCGA on 9/26/12
- Samples screened, 39 total sent that met TCGA qualifications
  - Exclusion criteria: Wilms tumor with radiation prior to thorascopy, recurrent mesothelioma, insufficient information on pathology report or only a cytology report available, another malignancy: sarcomatoid neoplasm, discrepancy between pathology report and current review, radiation treatment for prostate cancer, only lymph nodes reviewed by pathology, tumor nuclei percentage did not meet minimum requirement
- More samples have potential to be screened and sent at a later date to TCGA
Data Quality Assurance:

• Updating NMVB database
  - Added data to new fields created in NMVB database
  - Currently updating data on 65 cases for upcoming project

• Updated NYU database/ data
  - Updated and checked all our NYU Excel files to ensure all data is included in our main excel
  - Worked with Dr. Pass team to check our data files versus their records and worked to streamline data entry process including gaining access to many of their patient files to ensure utilized all information for data entry
Key Personnel:

- Raja Flores MD. (Surgeon/co-PI)
- Andrea Wolf MD. NMVB team leader announced Dec. 2012 (Surgeon & Investigator)
- Francine Dembitzer MD. (Pathologist)
- MaryBeth Beasley MD. (Pathologist)
- Janet Creason (Administration)
MSSM:

• Accruals:
  – Prospective Cases 10
  – Retrospective Cases 6

• Training:
  – Dr. Amin provided on site instructions to pathologist/data managers regarding annotation.
  – Two webinars provided additional training for clinical annotation and workflow processes.
Meso-Foundation Board of Directors:

- Michael Becich PhD
- Gen. Steven Blum
- Lee Krug MD
- David Ettinger MD
- Axel Ranier
- Richard Mosca
- Erica Iacono

- Terry Lynch
- Hanne Minz
- Michael Lagana
- Jocelyn Farrar DNP
- Ted Lackner
- Leon Pendarvis
Descriptors Board:

- Board Members are selected to represent the stakeholders in mesothelioma.

- Three attributes are considered of high importance: time, talent, and capacity to advance the mission.

- Advocates bring additional talent to board in addition to their personal relationship to the disease.
Scientific Advisory Board:

- Dr. Lee Krug
- Dr. Raffit Hassan
- Dr. Michele Carbone
- Dr. Steven Albelda
- Dr. Edward Levine
- Dr. Robert Taub
- Dr. Anne Tsao
- Dr. Petr Hausner
- Dr. Anna Nowak
- Dr. Steven Mutsaers
- Dr. Jeremy Steele
- Dr. Marc De Perrot
- Dr. Hedy Lee Kindler
Meso-Foundation Mission:

1. Unify the strong voices from patients and their families
2. Expand funding opportunities ($7.6 million in grants to researchers & $8.8 million from DOD)
3. Encourage collaboration among investigators (Annual Symposium, NMVB and Meso-SPORE collaboration)
4. Increase enrollment on clinical trials (Refers patients to appropriate centers for trials & establishment of clinical trials consortium)
5. Develop a patient registry
The Meso Foundation is the only 501 (c)3 non-profit

- The Meso Funds leading peer-reviewed research
- Provides complimentary educational and support resources
- Advocates for increased federal funding of mesothelioma research
NMVB Future Plans:

- NCI Meso-SPORE grant: result expected 1st Q 2013
  - Expansion: USCF, UHCC and Mayo Clinic and partnership with NCI
- Next Generation Sequencing (NGS) of Mesothelioma Cases @ U Pitt and The Cancer Genome Atlas (TCGA) partnership
  - Sharing over 200 mesothelioma cases with NCI
  - Comprehensive genomic characterization (old goal) for “free”
  - Will compare NGS with TCGA and create a portal to openly share this “deep phenotyping” NMVB provides with TCGA genomic & NGS data
- Considering further NMVB expansion:
  - Pacific Meso Foundation/UCLA (Bob Cameron) – 70 cases per year
  - The National Center for Vermiculite and Asbestos Related Cancers (NCVARC) (Mike Harbut) – Hundreds of highly characterized patients
  - Insulator’s Union Tissue Bank (MSSM – Andy Todd) – Screening studies
- Funding Future – What the Federal funding situation tells us...
Acknowledgment:

Collaborators:

- Center for Disease Control and Prevention (CDC)
- National Institute of Occupational Safety & Health (NIOSH)
- Mesothelioma Foundation (Meso Fndn)
- Mount Sinai School of Medicine (MSSM)
- New York University (NYU), New York City, NY
- University of Pennsylvania (U Penn), Philadelphia, PA
- University of Pittsburgh (U Pitt), Pittsburgh, PA

Future Partners: NCI Meso SPORE Core to NMVB in 2013 with the University of Hawaii (UHCC) via Meso SPORE to also include Mayo and UCSF as well as Insulator’s Union Tissue Bank @ MSSM.

Leadership:

Steven Abelda, MD (U Penn)  James Luketich M.D (U Pitt)
David Bartlett, MD (U Pitt)  Jonathan Melamed MD (NYU)
Michael J. Becich MD, PhD (U Pitt)  Harvey I. Pass MD (NYU)
Michael Feldman MD (U Penn)  Arjun Pennathur, MD (U Pitt)
Mary Hesdorfer (Meso Fndn)  James Pingpank, MD (U Pitt)
Raja Flores, MD (MSSM)  Andrea Wolf, MD (MSSM)
Francine Dembitzer, MD (MSSM)  Mary Beth Beasley, MD (MSSM)
Mesothelioma Tissue Resources Available for Your Research

MVB database version 2.0 has been released that provides researchers real-time access to demographic, epidemiologic, pathologic, genotype, and follow-up data associated with biospecimens at no cost. Researchers interested in utilizing NMVB samples for their research may submit an application. All researchers (academic or commercial, United States or foreign) may apply for NMVB tissue specimens.

NMVB currently has 837 annotated cases and 1014 biospecimens including:

- Paraffin Embedded Tissue
- Fresh Frozen Tissue
- Blood and DNA Samples

The NMVB also has developed mesothelioma tissue microarrays (TMAs) with associated multimodal data annotation. Additional TMAs will be available shortly — please sign up for our mailing list if you would like to be notified when TMAs are available for order.

http://www.mesotissue.org/
Marketing Efforts:

NMVB resource has been marketed in the following major meetings:
- United States and Canadian Academy of Pathology (USCAP)
- American Medical Informatics Association (AMIA) – won award
- American Association for Cancer Research (AACR)
- Meso Foundation Annual Meetings (2006 to 2012 and beyond!!!)
- Pathology Informatics (2009 & 2011) - won award

Publications by NMVB team to date:


Publications (Abstracts):


NMVB Research Staff:

U Penn:
Fred Valdiviesco
Nicole Lunceford

U Pitt:
Michelle Bisceglia
Tina Tmoko
John Milnes
Julie Wards
Patricia Williams
Althea Schneider
Marianne Notoro

NYU:
Audrey Sorensen
Samantha Lincoln
Monica Gorman
Ruth P. Benito
Ryan Harrington

MSSM:
Janet Creason
Katina Summerford
Steven Grossman
Stacy Heath
Thank You