LEVERAGING NMVB FOR DISCOVERY RESEARCH

(HTTPS://WWW.MESOTISSUE.ORG)
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Advocacy Partner – Meso Foundation (HTTP://WWW.CUREMESO.ORG)
(DISCLAIMER – Board Member of Meso FnDn)
Updates to NMVB – Newest Team Members

• New team members;
  • Faina Linkov, PhD – Associate Professor of OB/Gyn and Epidemiologist – funded by Text Information Extraction System (TIES) Cancer Research Network (TCRN, NCI ITCR grant)
    • Works with NMVB team on ways to promote scientific impact
    • Co-author on two papers under review
  • Melissa Schwenk, MS – Research Assistant
    • Works collaborative on outreach and communications for both TCRN and NMVB
    • Has improved social media presence of both projects
  • Jonathan Silverstein, MD MS – Chief Research Informatics Officer (CRIIO) for DBMI
    • Runs the Research Informatics Office (http://rio.pitt.edu/services) and the Research Records Request (R3) system http://rio.pitt.edu/policy-and-procedures
    • Holds Business Associate Agreement (BAA) for UPMC data
TIES Cancer Research Network (TCRN)

UPMC Hillman Cancer Center (lead)
- Augusta University Cancer Center
- Abramson Cancer Center (Penn)
- Roswell Park Cancer Institute
- Stonybrook University (new partner)
- Sidney Kimmel Cancer Center (TJU)
- 13 Cancer Centers interested in joining
  - Including NYU – part of NMVB network

Network Trust Agreements
- IRBs agree that use of data for investigators is Not Human Subjects Research, no need for an additional IRB protocol even to access record level de-id data
- Governance
- Agreement to abide by SOPs
- Instrument of Adherence

Soliciting new WSI “ready” partners!

http://cancerdatanetwork.org
A Federated Network for Translational Cancer Research Using Clinical Data and Biospecimens

Rebecca S. Jacobson¹, Michael J. Becich¹, Roni J. Bollag², Girish Chavan¹, Julia Corrigan¹, Rajiv Dhir¹, Michael D. Feldman³, Carmelo Gaudioso⁴, Elizabeth Legowski¹, Nita J. Mahle², Kevin Mitchell¹, Monica Murphy⁴, Mayurapriyan Sakthivel⁴, Eugene Tseytlin¹, and JoEllen Weaver³

Abstract

Advances in cancer research and personalized medicine will require significant new bridging infrastructures, including more robust biorepositories that link human tissue to clinical phenotypes and outcomes. In order to meet that challenge, four cancer centers formed the Text Information Extraction System (TIES) policies, and procedures, enable regulatory compliance. The TIES Cancer Research Network now provides integrated access to investigators at all member institutions, where multiple investigator-driven pilot projects are underway. Examples of federated search across the network illustrate the potential impact on

http://cancerdatanetwork.org
The Path Ahead for NMVB (modified from 2017):

- **Cancer Institute of New Jersey**
  - Richard Alexander, MD U MD surgeon now at CINJ has voiced interest

- **Genomic (whole genome sequencing) for NMVB**
  - Still looking for industry and/or philanthropic partner (may engage UPMC Clinical and Research Genomics Center)

- **Patient-Centered Mesothelioma Data Sharing**
  - How do we move to a more modern architecture for data sharing?
  - No progress on National Mesothelioma Registry – Meso Fndn changes

- **Tapping into the Precision Medicine Initiative**
  - Leverage Pitt’s PA CARES for US

- **Partnering with People Centered Research Foundation**
  - PaTH (Pitt/DBMI’s) Mid Atlantic Network is “tier 1” site visit 6/13

- **Support Interactome Studies as new NMVB data sharing**
  - Ganapathiraju Presentation Today – Add as a resource to NMVB portal

- **Sustainability**
  - The big unanswered question
  - Partner with Meso Fndn or separate 501c3?
The National Landscape – NMVB Opportunities

- **Patient Centered Outcomes** Research Institute (PCORI) becomes the People Centered Research Foundation (PCRF)
  - DBMI hosts the PaTH Network (Geisinger, Hopkins, Penn State and Temple) focused on creating a Learning Health System
  - Goal is to enroll patients in comparative effectiveness and pragmatic clinical trials and collect patient reported outcomes (REDCap)

- **Accrual to Clinical Trials** (ACT) – NCATS CTSA effort
  - DBMI developed laboratory and medication ontology and data model for this network of 31 sites which will grow to 62 sites in next 3 years

- **Precision Medicine** Initiative at Pitt
  - DBMI host the PA All of US program of the All of US program
  - Goal to enroll 150,000 patients at Pitt (Clinical and Research Sequencing Center by UPMC) and do Whole Genome Sequencing on 1M patients for data sharing nationally
PCORI PaTH and NCATS ACT are Unlocking Clinical Data from EHRs

Key Drivers for Precision Medicine Initiative

Patient Data & UPMC – De-identified Research Data Warehouse
Shyam Visweswaran, MD PhD – http://www.act-network.org
and Mike Becich, MD PhD - http://pathnetwork.org
Result = a clinical research data warehouse @ Pitt/UPMC

ACT Site Distribution

ACT
- Accrual to NIH Clinical Trials
- Common informatics platform
- Investigator-driven queries
- Patient/community engagement through CTSA

PCORNet
- Clinical Effectiveness (may include trials)
- Different informatics platforms linked centrally
- Central queries

Result = Computable Phenotypes & a Learning Health System

- PaTH – Geisinger, Hopkins, Pitt, Penn State, UPMC, Utah & Temple (11M)
- ACT – 20+ CTSA sites–Data Harmonization led by Pitt (37M)
- Fueled forward by Precision Medicine Initiative (150K patients to be enrolled)

SI
Department of Biomedical Informatics
New York and Pennsylvania each were funded and will enroll over 350,000 patients.

Time for action to leverage this 1M patient cohort and its focus on genomics and biospecimens.
NMVB Related and Supported Publications:


3. Ganapathiraju presentation at International Mesothelioma Interest Group (IMIG) on Interactome Analysis (poster in hallway)

4. Pending Publications:
   - NMVB Cohort Survival Analysis – resubmitted
   - Mesothelioma Interactome Analysis – pending submission
   - Mesothelioma Whole Exome Sequencing in Pleura and Peritoneum – pending submission
The NMVB Team
Thanks you!!!
E-mail becich@pitt.edu for publication reprints, LOI forms and protocols.
Possible NMVB/TCRN Collaboration – TILs in Meso

Spatial Organization and Molecular Correlation of Tumor-Infiltrating Lymphocytes Using Deep Learning on Pathology Images

Tumor-infiltrating lymphocytes (TILs) were identified from standard pathology cancer images by a deep-learning-derived “computational stain” developed by Saltz et al. They processed 5,202 digital images from 13 cancer types. Resulting TIL maps were correlated with TCGA molecular data, relating TIL content to survival, tumor subtypes, and immune profiles.

Highlights

- Deep learning based computational stain for staining tumor-infiltrating lymphocytes (TILs)
- TIL patterns generated from 4,759 TCGA subjects (5,202 H&E slides), 13 cancer types
- Computationally stained TILs correlate with pathologist eye and molecular estimates
- TIL patterns linked to tumor and immune molecular features, cancer type, and outcome

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Graphical Abstract

Cell Reports, 2018

NCI ITCR Funded U24 CA180924 (Saltz and Sharma), U24 CA215109 (Saltz and Prior) and others
Tumor Heterogeneity Research Interactive Visualization Environment (THRIVE – NCI ITCR U01 @ Pitt)

- Computational Pathology
  - Hyperplex Immunofluorescence (9 to > 50 Ab)
  - Machine Learning + Spatial Statistics
  - Network Systems Biology
  - Partnership with General Electric (GE)
- Iterative experimental–computational tumor micro-environment studies

Courtesy Chakra Chennubhotla, 2017
NCI ITCR funded effort (U01 CA204826)
Platform for Quantitative Evaluation of Spatial Intratumoral Heterogeneity in Multiplexed Fluorescence Images

Daniel M. Spagnolo¹,², Yousef Al-Kofahi³, Peihong Zhu³, Timothy R. Lezon²,⁴, Albert Gough²,⁴, Andrew M. Stern²,⁴, Adrian V. Lee⁵,⁶, Fiona Ginty⁷, Brion Sarachan³, D. Lansing Taylor²,⁴,⁵, and S. Chakra Chennubhotla²

Abstract

We introduce THRIVE (Tumor Heterogeneity Research Interactive Visualization Environment), an open-source tool developed to assist cancer researchers in interactive hypothesis testing. The focus of this tool is to quantify spatial intratumoral heterogeneity (ITH), and the interactions between different cell phenotypes and noncellular constituents. Specifically, we foresee applications in phenotyping cells within tumor microenvironments, recognizing tumor boundaries, identifying degrees of immune infiltration and epithelial/stromal separation, and identification of heterotypic signaling networks underlying microdomains. The THRIVE platform provides an integrated workflow for analyzing whole-slide immunofluorescence images and tissue microarrays, including algorithms for segmentation, quantification, and heterogeneity analysis. THRIVE promotes flexible deployment, a maintainable code base using open-source libraries, and an extensible framework for customizing algorithms with ease. THRIVE was designed with highly multiplexed immunofluorescence images in mind, and, by providing a platform to efficiently analyze high-dimensional immunofluorescence signals, we hope to advance these data toward mainstream adoption in cancer research. Cancer Res. 2017 Nov 1;77(21):e71-e74. ©2017 AACR.

Cancer Res. 2017 Nov 1;77(21):e71-e74. doi: 10.1158/0008-5472. PMID: 29092944

NCI ITCR funded effort (U01 CA204826)