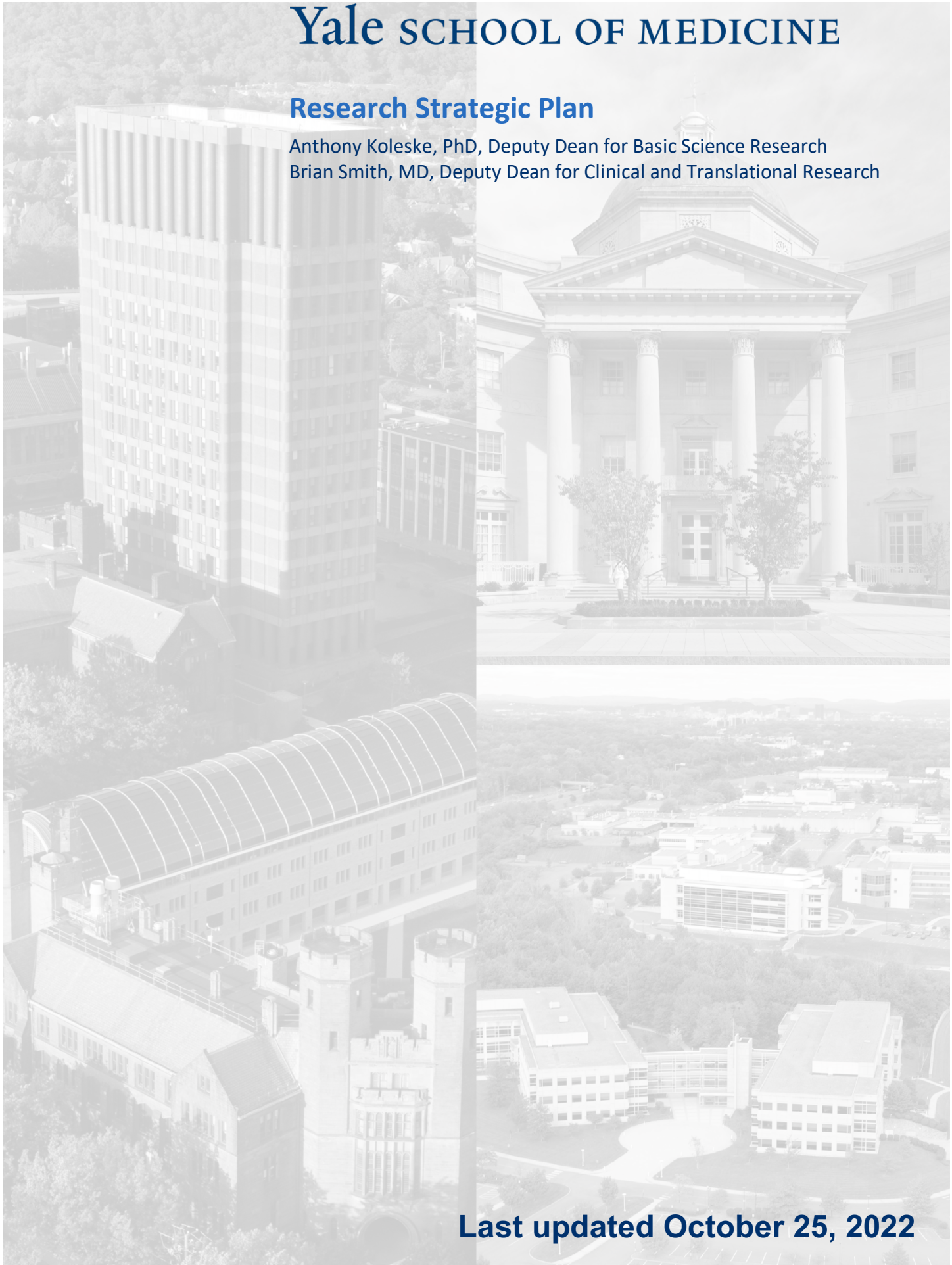

Yale SCHOOL OF MEDICINE

Research Strategic Plan

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Research Strategic Plan Summary

The University Science Strategy Committee identified the most promising opportunities for university-wide investment across scientific disciplines. Building on this effort, Yale School of Medicine has developed a strategic plan for scientific research that aligns with the broader plan and builds on key strengths in the school.

The strategic planning process began with one-on-one interviews with more than 80 faculty members who were identified by chairs, center directors, and deans as the future leaders of YSM. The interviews focused on three big questions:

- "What are the big research questions/goals that you would like to focus on at YSM in the next decade?"
- "Who are the colleagues with whom you would work and if we lack the requisite expertise, whom should we be recruiting?"
- "What are the obstacles, either infrastructural or procedural, that might impede progress?"

These questions led to the formation of eight focused discussion groups, each tasked with developing a strategic plan in a given area. These plans were presented at the November 2020 Chair's Retreat and were prioritized for future planning based on extensive discussion among this leadership group. The plan recommends **three areas for cross-cutting themes**, **eight focused areas of research**, and **ongoing investments in institutional infrastructure** essential to meet this vision.

Cross-Cutting Themes

The School of Medicine has identified three cross-cutting themes that will support basic, translational, and clinical researchers across the organization.

Data Science

A strategic investment to expand our presence in Data Science, which is integral to all areas in biomedical sciences, is recommended to ensure sustained scientific excellence.

- Create a new section/department in biomedical informatics and data science as a home for faculty experts in all areas ranging from clinical informatics to bioinformatics and data science
- Expand in areas that may include:
  - Biomedical/health record data (computational health)
  - Image processing
  - Next generation "omics" (single cell, integration across platforms, other)
- Develop infrastructure for core support in this area
  - Organize communities with shared approaches and interests
  - Create the Yale-Boehringer Ingelheim Biomedical Data Science Fellowship Program

Team Science

A strategic investment to foster collaboration and large-project team science is recommended to continually facilitate innovation and interdisciplinary science.

- Set up organizational structure to facilitate teams in large initiatives/team science

- Provide pilot funding program to support nascent teams to develop high impact projects
- Facilitate exposure of faculty new to the YSM and Yale community via research-in-progress presentations and networking

Support for Graduate Students and Postdocs

A strategic investment to support graduate students and postdocs is recommended to provide new opportunities and paths for these trainees.

- Create new opportunities for endowed slots for students and postdocs
  - e.g., new Tsai Institute proposal contains slots for students and postdocs
  - Continue the commitment from GSAS, provost, and YSM for 35% tuition matching for graduate students

- Create new paths for training PhD students in clinical departments
  - Create a process to appointment faculty in clinical department directly to the graduate school
  - Create a new PhD track in translational biomedicine

- Enhance postdoctoral training
  - Establish new postdoc office
  - Standardize and provide programming to enrich postdoc experience
  - Enhance training in career skills
  - Make Yale a “postdoc destination”

- Expand and enhance our culture of inclusive excellence
  - Standardize search processes and optimize them to identify talent broadly
  - Inaugurate the YSM Science Fellows program for junior scientist-to-faculty development
  - Compete successfully for NIH FIRST proposal for cluster hires in neuroscience, metabolism, and health equity

Focused Areas of Research

The School of Medicine has identified eight focused areas of research that build upon existing strengths and leverage opportunities for collaboration and interdisciplinary science.

Inflammation: A Multidisciplinary Approach

- Create a hub and spoke model for an Institute of Inflammation Science
  - Microbiology/microbiomics, neuroscience, cardiovascular biology, clinical medicine, modeling/data science, biomedical engineering, and systems biology

Single Cell Biology

- Build on strengths in nuclear cell biology, epigenetics, and single cell biology
- Recruit cohort with a concentration of expertise in single cell biology
- Support groups already working together on program project-type applications
- Synergize with investments in key technologies and data science

- Seize opportunities for collaborative team projects that span departments and disciplines

Metabolism

- Establish the Yale Center for Molecular & Systems Metabolism
- Integrate with Diabetes Center, Liver Center, and Vascular Biology & Therapeutics

Developmental Brain Disorders

- Bring together strength distributed across many departments and centers
- Seize opportunities for collaborative team projects that span departments and disciplines

Health Equity Research

- Leverage appointment of Marcella Nunez-Smith, MD, MHS, as inaugural associate dean of health equity research to coordinate efforts across the school and create common tools
- Enhance positions in YCCI and Yale Cancer Center devoted to health equity research
- Support the SEICHE Center for Health and Justice (Yale School of Medicine plus Yale Law School)
- Include as a targeted area for cluster hiring in our FIRST Award application

Technology and Biomedical Engineering (most expensive of proposed initiatives)

- Facilitate joint hires in data science, biomedical engineering, and computer science
- Recruit faculty in cutting edge technologies (mass spec, FIB-SEM, imaging)

Biomedical & Biological Imaging

- Recruit new PET Center director; continue the transformative initiative that the PET Center has been, and simultaneously enhance its service role
- Organize and brand an umbrella center to facilitate collaboration and serve as a home for program/center grants and training grants
- Identify opportunities to better connect biomedical and basic biological imaging (example: FIB-SEM)

Translational Medicine/Clinical Trials

Strengthen support for broad infrastructure needs in light of changing NIH priorities and funding in this area. Develop plans in this area built on a framework designed to enlist more members of underrepresented groups as participants in clinical trials, an approach enhanced by the successful renewal of the CTSA.

- Create faculty advisory groups to provide input to YCCI functions across inpatient and outpatient needs
- Collaborate to create a health-system-wide common IRB, common infrastructure, sample collection to create a true “learning health system”

- Improve feasibility evaluation to concentrate resources on highest-priority trials, improved recruitment for clinical trial personnel, workforce development
  - Establish formal Education in Clinical Trials Research, including MSCI program
  - Accelerate clinical trial activation
  - Establish chief research information officer role

Institutional Infrastructure

The School of Medicine is committed to making strategic investments in institutional infrastructure to support discovery and facilitate access to essential tools and resources.

Office of Team Science (OTS)

- Create OTS to promote assembly of teams and manage projects to submission of P and U type NIH grants. Provide pilot funding for teams to nucleate new proposals via the newly formulated Program for the Promotion of Interdisciplinary Team Science (POINTS) Program.

Biorepository

- Create the YSM Biorepository as a central coordinated biorepository that allows for the alignment of collected tissue, plasma, serum and genetic samples and clinical data, using common processes and information systems.

  - Integrate live tissue and cell collection, molecular banking with clinical data management
  - Provide a systematic means to interrogate, access samples
  - Provide a platform to coordinate all existing Yale tissue banks
  - Achieve College of American Pathologists (CAP) accreditation

APPENDIX A

Executive Summary: Task Force on Inflammation, Metabolism, Cancer, And Disease

Committee Members: Marcelo Dietrich (co-chair), Rachel Perry (co-chair), Ranjit Bindra, Vishwa Deep Dixit, Stephanie Eisenbarth, Andrew Goodman, Carla Rothlin, Yajaira Suarez, Andrew Wang

Energy metabolism is the principle underlying all biological processes, broadly affecting health and disease. Yale School of Medicine is home for an outstanding body of expertise surrounding the topic of energy metabolism research, spanning from molecular to clinical research. The task force therefore identified the broad field of energy metabolism as an area for strategic investment in the short- and long-term. Moreover, and equally important, energy metabolism at the cellular and organismal levels is directly influenced by nutrition, an area of research that the task force concurs is in need of major progress. Yale is poised to move to the forefront of these areas of investigation.

We propose to create an **Interdisciplinary Initiative in Metabolism** that will serve as a hub, uniting dynamic and collaborative networks of inquiry (see **Figure 1**). The goal of this initiative is to promote cross-disciplinary research exploring the basic biology of metabolic regulation from molecules to organisms as well as the effects of nutrition on metabolic regulation in health and disease.

The task force supports the following guiding principles for the **Interdisciplinary Initiative in Metabolism**:

- Long-term commitment with stability of funds and support;
- Provision of administrative oversight;
- Close relationship with the Office of Development to maximize fundraising;
- Support for state-of-the-art core facilities that are accessible to all faculty;
- Support of new, high-risk collaborations, in the frontier of sciences;
- Minimize interdependence on departments, reporting directly to the Dean's Office.

The task force identified a major opportunity for long-term, stable support of collaborative research on metabolism, supporting existing and emerging initiatives at YSM. In this vein, the task force identified two areas of focus for immediate investment: Cellular Metabolism and Body-Brain Systems. In addition, the task force identified a broad area for future leadership and long-term investment: Mechanisms of Food, which relates to the study of the chemical, molecular, and system-level mechanisms by which different food affects health and predisposes to disease. This area of study will involve strong cross-pollination between disciplines, from structural and chemical biology to clinical medicine.

We propose the following activities under the **Interdisciplinary Initiative in Metabolism**:

- Upgrade and democratization of Core Facilities related to energy metabolism research at YSM.
- Provision of strong Administrative Support for Core Facilities and Large Grant Applications.
- Fundraising campaign with continuous conversation between faculty and the Office of Development.
- Creation of two Centers of Excellence on Metabolism Research, selected on a competitive basis, for a 6+6 years period, grouping 4-8 faculty, focused on Cellular Metabolism and on Body-Brain Systems.

- Funding of Collaborative Team Awards to foster inter-disciplinary collaborations (generous funding for 3 years).
- Funding of a Training Grant on Metabolism Research.
- Provision of executive coaching for teams to develop a long-term vision, maximize fund raising, and success in large grant applications.

In sum, the **Interdisciplinary Initiative in Metabolism** will allow Yale to leverage its existing strengths to entrench and extend its leadership in metabolism, inflammation, cancer and disease (see **Figure 2** for a timeline of deliverables). This Initiative will turn silos of expertise into cross-disciplinary research endeavors, at which Yale will be well-positioned to be at the forefront.

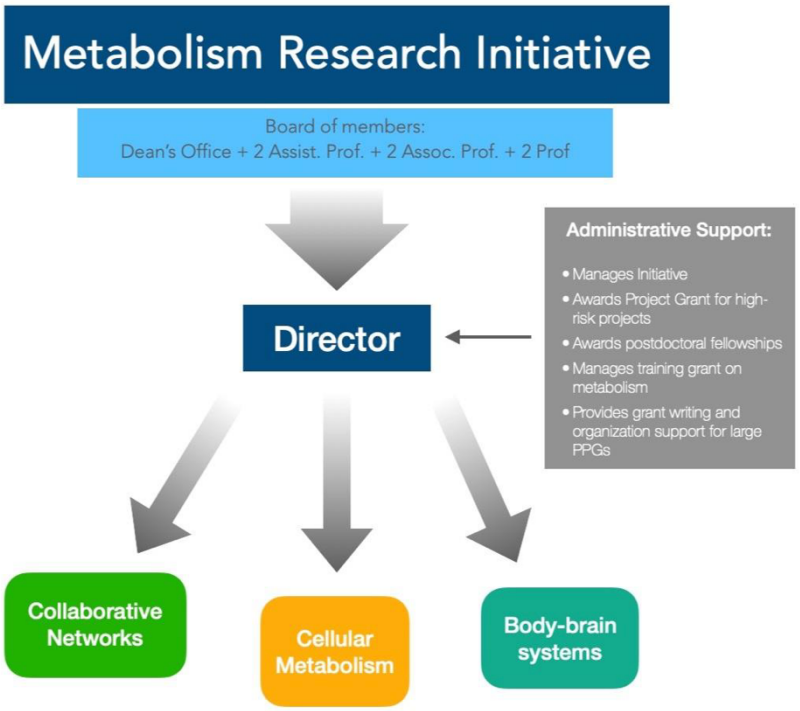

Figure 1 Proposed structure of the Interdisciplinary Initiative in Metabolism.

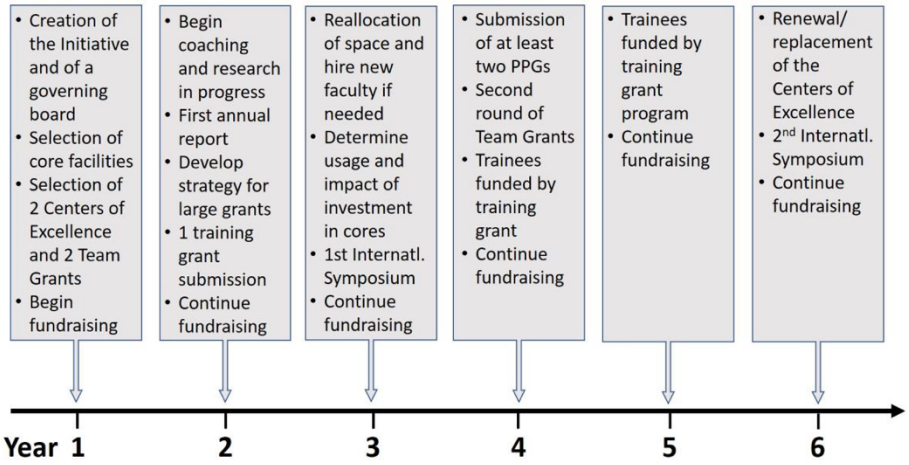

Figure 2. Timeline and deliverables for the proposed Interdisciplinary Initiative in Metabolism.

APPENDIX B

YSM Strategic Planning on Nuclear Cell Biology, Epigenetics, and Single Cell Biology

Committee Members: Qin Yan (co-chair), Shangqin Guo (co-chair), Peggy Myung, Yajaira Suarez, Andrew Xiao, Steven Wang, Patrick Lusk, Christian Schlieker, Zachary Smith, Brian Hafler, Lauren Sansing

Topic of your Committee: Imaging and sequencing-based spatial omics, chromatin trafficking/signaling, technology and bioinformatics need.

Summary of group members and process for discussion: The question that unites the research interests of our group could be said as "how does one linear genome lead to diverse biological phenotypes/pathology?". Our group collectively need to be able to observe, perturb and quantify the behaviors of single genomic elements and/or single nucleus/cells effectively, across diverse biological contexts and disease settings.

The group has three major areas of interest/expertise: 1) cell biological understanding of the nucleus (nuclear envelope, chromatin organization: Patrick, Christian, Steven, Shangqin); 2) epigenetics (chromatin and DNA modification: Qin, Andrew, Zack) and 3) diseases-oriented systems to understand how individual cells respond and communicate (Brian, Lauren, Peggy, Yajaira, Qin, Shangqin). These interests are crossing large scales and realms of biology, from potentially single molecular complexes (nuclear pores), to single nucleus (single cell epigenomics, scRNA-seq), to tissue level cell organization/dynamics. Some group members have been collaborating and are planning for team projects. The group had three zoom meetings and discussed by emails and google document to set up a strategic plan in this area, focusing on the key areas that YSM can lead, team projects and core facilities necessary to achieve these goals.

Overall assessment and recommendations: Nuclear Cell Biology, Epigenetics, and Single Cell Biology are areas of emerging importance with existing strength at Yale, in particular on nuclear envelope biology, chromatin biology, and single cell transcriptomics. However, Yale has NOT been recognized as a leading institution in these areas. The working group recommended to establish a Center for Nuclear Cell Biology and Epigenetics (name to be refined) to synergize our efforts in key areas, to facilitate and support the utilization of cutting edge imaging and bioinformatics approaches via potential new core facilities overseen by faculty level scientists. Only when the necessary technologies are made available and affordable to most Yale teams,
Yale labs can widely benefit from the new tools to address fundamental and disease-related questions using cancer, stem cell/development, and neuronal systems, among others, as the testing platforms.

Arenas - What type of research activity should we engage in?

1) 3D chromatin organization, including dynamics and kinetics, and its interplay with/by DNA and histone modifications as well as transcription factors, and their implications in development and diseases. This can be studied with imaging/sequencing-based spatial transcriptomics, in combination with other omics approaches.
2) Mechanisms of cytosolic DNA formation and its roles in cancer and immune signaling/inflammation. This is an emerging field and could be an area of focused recruitment. Junior scientists from the labs of Paul Mischel, Roel Verhaak, and Vineet Bafna could be

considered. This could interface well with our existing strength on nuclear envelope biology and mechanical regulation of the chromatin.

3) Novel technology development, with a focus on nuclear/chromatin imaging. Nuclear imaging inherently generates single cell-based information. Applied to live cells, it could also yield dynamic and kinetic information, bridging points 1&2 above. This area also has the potential to bridge sequenced-based and image-based genomics approaches. Mid-career and junior scientists from the labs of Tjian & Darzacq, Taekjip Ha, Job Dekker, Leonid Mirny, Bing Ren, Edith Heard or Sunney Xie could be considered.

Vehicles and Process - How will we get there? Who are the players and collaborations? In what areas do we need to make hires? What infrastructural support do we need?

1) Organize and strengthen what we already have. We need to establish a center to bring together the groups to build P01 and potentially U54/U01 projects on "Nuclear cell biology and epigenetics across scales", with workshops and retreats to foster interactions, pilot funding, grant writing support and faculty level hires in the key research areas for program project development (see **Appendix A** for potential projects). DBiT-Seq for high-spatial-resolution multi-omics sequencing developed by Rong Fan should be quickly adopted.
2) Build/develop what is needed by many. The group expressed **urgent need** for support in two specific areas: bioinformatics and high-end imaging cores. These cores should be run by faculty level scientists whose success is not measured by grant funding support, but by their instrumental support to Yale's research community. Staff scientists could be an alternative. The mission of these cores should be to stay abreast with cutting-edge technologies and to propagate such technologies to the Yale community (i.e. "democratization").

The bioinformatics core should be able to help any/most lab in need to analyze single cell/spatial transcriptomics/epigenomics and integrative analysis with proteomics and metabolomics (could be advised by Yuval Kluger and/or Smita Krishnaswamy). This is a fast-evolving field, both in assay development and data analysis. Single cell transcriptomics analysis is widely used by YSM labs, but Yale is far behind the competing institutions on the supporting infrastructure for data analysis. The burden on individual labs to apply the technologies effectively and timely is prohibitively high.

High resolution imaging core should have the capability to look deep in the nucleus. While Yale has leaders in the development of super resolution platforms (e.g. Jöerg Bewersdorf), access to high-end commercial super-resolution microscopy platforms is challenging. There is an opportunity to lead in this arena with the recruitment of additional faculty and lowering costs to access instrumentation. Complementing cryo-EM based approaches, imaging-based spatial genomics and transcriptomics need to be enhanced. For example, Steven Wang has a long list of 30+ collaborators, but suffers from inadequate instrument time to support the wide need. A core facility that replicates his system and has complementary capability would greatly advance these projects.

Furthermore, the group emphasized the importance for these cores to educate/train individual labs to make the technologies readily accessible across fields and levels of expertise, enabling Yale's teams to stay at the forefront to capitalize on new technologies.

Differentiation - What advantages/assets already exist at Yale in this field? How will YSM distinguish itself or lead in these areas? How will we become recognized for that?

To lead in these areas, Yale investigators need to have easy, affordable access to cutting-edge technologies, test their discoveries in these areas with functional studies using platforms that are strong at Yale including cancer, stem cell biology and neurodegeneration, bridging basic and clinical

science. Successful epigenetic centers (UPenn, UCSD, Broad, MD Anderson, UNC, Northwestern) focused on basic science and technology development.

Products - What are our deliverables? How will we know if we are successful in this area?

1. Established a Center for Nuclear Cell Biology and Epigenetics (name to be refined) with defined focus areas (see tentative areas in **Appendix A**), supported by multiple-P01, U54/U01, and multi-PI R01 grants.
2. Identified/Hired scientist(s) to lead the imaging and bioinformatics cores. The Cores are meeting, or working to meet, the need of Yale's research community.
3. Contributed novel technologies to the larger research community.
4. Accelerated pace of discovery, measured by original publications and funding support.
5. Promoted synergy and collaboration across biology/diseases, basic, translational and clinical, and scale (genomic sequence/molecule→cell behavior→organismal biology).
6. Obtained training grant(s) to prepare the next generation of scientists.

Timeline - If we were to have an impact in this area in 5 years, what is timeline on deliverables to achieve this?

1. Year 1, establish Center for Epigenetics and Nuclear Cell Biology (see **Appendix B** for core Epigenetics Interest Group). Years 1-5, use the center as the platform to organize annual retreats/symposia and periodic workshops to foster collaborations; promote Yale faculty/trainees to speak at national and international conferences and compete for awards to improve reputation.
2. Years 1-2, targeted recruitment in nuclear/chromatin imaging and cytosolic DNA to further support program and core project development and establish critical mass in these core areas of research.
3. Years 1-2, expand capacity of our existing expertise and enhance access to technologies with the help of dedicated staff/faculty. Years 3-5, expand this core with P01 and P30 grants (see below).
4. Years 1-2, backed by pilot funding, grant writing support and investment for cores from YSM, submit 2-3 program project applications and several multi-PI R01 grants.
5. Years 3-5, submit 3-5 additional program project applications, one P30 center core grant, 1-2 training grants, and several multi-PI R01 grants. These grant applications should benefit from the newly recruited investigators and expanded "4D Imaging/Genomics core". By year 5, we should have secured at least 2-3 program projects, one P30 center core grant, one training grant and several multi-PI R01 grants.

Appendix A: Potential program project proposals and example synergy

1. <u>Epigenetic mechanisms of resistance to cancer therapies (supported by YCC Team Challenge Award)</u>
   - **Project 1:** (PI: Politi) Epigenetic control of tumor cell plasticity and drug tolerance in EGFR mutant lung cancer
   - **Project 2:** (PI: Xiao) Epigenetic regulation of TKI resistance by the N^6-mA DNA modification
   - **Project 3:** (PI: Yan) Targeting KDM5 histone demethylases to overcome resistance to trastuzumab+ pertuzumab combination therapy
   - **Project 4:** (PI: Guo) Timing live cell cycle length to dissect mechanisms of AML chemoresistance

2. <u>Modulating Epigenetics to Enhance Antitumor Immunity (supported by YCC Team Challenge Award)</u>

Project 1: (PI: Yan) Epigenetic suppression of antitumor immunity by KDM5B histone demethylase
Project 2: (PI: Bosenberg) Regulation of antitumor immunity by H3K9 methylation
Project 3: (PIs: Iwasaki and Ishizuka) Enhancement of antitumor immunity by endogenous retrovirus expression

3. Epigenetic Regulation of Breast Cancer Metastasis

Project 1: (PI: Yan) Targeting acetylation reader CECR2 to modulate breast cancer metastasis
Project 2: (PI: Nguyen) Epigenetic regulation by WDR5 in breast cancer metastasis
Project 3: (PI: Guo) Activating MKL1/SRF pathway to target breast cancer metastasis

4. Examining the intersection of development and disease across tissues at the multiscale level

Project 1: (PI: Myung): Dissecting the molecular origins of hair follicle induction during development, adult regeneration, and disease
Project 2: (PI: Hafler): Examining the genomic underpinnings of retina development and age-related macular degeneration
Project 3: (PI: Smith) Mapping the Epigenetic and transcriptomic changes that define early segregation of cell fates during development and that are dysregulated during aging/cancer
Project 4: (PIs: Wang and Xiao) Investigating 3D nucleome and gene expression regulation via N^6-mA DNA modification in embryonic development and cancers
Project 5: (PIs: Wang and Hafler) Mapping the 3D nucleome and transcriptome changes in neurodegenerative diseases in human brains and retinas
Project 6: (PI: Sansing) Epigenetic and transcriptomic contributions to progression of cerebrovascular diseases (needs spatial transcriptomics/imaging)

5. Nuclear envelope dynamics and assembly across evolution.

Project 1: (PI: Bahmanyar) Nuclear envelope identity and dynamics in the early embryo
Project 2: (PI: King) Phase-separation as a foundation for nuclear mechanics
Project 3: (PIs: Guo and Lusk) Re-establishing nuclear architecture after mitosis

1. Crosstalk between chromatin biomechanical regulation and tissue patterning

Project 1: PI: King) The role of LINC complex in directing SMAD-based chromatin events
Project 2: (PI: Guo) Chromatin regulation by the mechanotransduction pathway in pluripotency
Project 3: (PI: Fan) Microfabrication to enable spatiotemporal patterns of mechanical and biochemical cues to inform mechanobiology
Project 4: (PI: Sozen) Mechanotransduction in early embryonic development and patterning
Project 5: (PI: Sumigray) Mechanotransduction in tissue morphogenesis using organoid culture

2. Mechanisms of cytosolic DNA formation and its roles in cancer and immune signaling/inflammation

Project 1: (PI: Lusk) Mechanisms of selective DNA capture across the nuclear envelope barrier
Project 2: (PI: King) Clearance of episomes during meiosis

Project 3: (PI: Xiao) N6-mA methylated DNA in the cytosol
Project 4: (PI: Rothlin) Cytosolic-DNA-mediated triggering of innate immune signaling

3. New paradigms of nuclear transport and nuclear quality control in neurological disease

   Project 1: (PI: Schlieker) Pathological mechanisms of nuclear pore formation in neurological disease
   Project 2: (PIs: Lusk, Schlieker and Melia) Mechanisms of nuclear envelope turnover in neurons
   Project 3: (PI: Lusk) Quality control of nuclear pore injury in C90RF72 ALS
   Project 4: (PI: Koleske) Impact of nuclear pore-related deficits in mouse brain development

4. Appendix B. Epigenetics Interest Group with monthly seminar series (established by Qin Yan in 2010)

15 participating labs (7 departments across all three Yale campuses):

Nadya Dimitrova (MCDB)
Patrick Gallagher (Pediatrics, Genetics and Pathology)
Antonio Giraldez (Genetics)
Yannick Jacob (MCDB)
Megan King (Cell Biology and MCDB)
Bluma Lesch (Genetics)
Morgan Levine (Pathology and Epidemiology)
Haifan Lin (Cell Biology, Genetics and OBGYN)
David Schatz (Immunobiology and MB&B)
Matthew Simon (MB&B)
Siyuan (Steven) Wang (Genetics and Cell Biology)
Sherman Weissman (Genetics)
Josien van Wolfswinkel (MCDB)
Andrew Xiao (Genetics)
Qin Yan (Pathology)

APPENDIX C

Bridging Clinical and Research Efforts Across Levels and Spanning Yale

Committee Members: Miriam Treggiari (co-chair), Stuart Weinzimer (co-chair), Steven Bernstein, Onyema Ogbuagu, Stephanie O'Malley, Dan Petrylak, Uma Reddy, Jerry Sanacora, Eugene Shapiro, Eric Velazquez

Yale Center for Neurodevelopmental Disorders (YCND)

Yale has tremendous expertise in clinical and basic research targeting normal and abnormal development of the nervous system, but these efforts are largely fractured across sub-disciplines. **Our goal is to create a transformative, synergistic center focused on neurodevelopmental disorders, spanning multiple levels of analysis (genetic, molecular, cellular, circuits, behavior) and harnessing the diverse elements of the Yale research community.** To meet this challenge, we will build a comprehensive Yale-wide pipeline for coordinated clinical and basic research designed to identify the mechanisms underlying convergent phenotypes in neurodevelopmental and neuropsychiatric disorders. This program will bridge work in multiple species (human, mouse, zebrafish) and from genotype to phenotype in an unprecedented framework for transformative research organized around four Clusters of Effort:

Cluster 1: Human Neural and Behavioral Phenotyping

In order to support sharing of data across clinical and basic research projects, we need to collect in-depth phenotypic data from patients with neurodevelopmental disorders across multiple time points and connect those data to underlying genotypes. Specific clinical assays should match those carried out by basic research groups, and the resulting database must be accessible to both clinical and research laboratories across the Yale community. In addition, these novel efforts should produce negligible increases in participant burden. To meet these criteria, phenotyping will comprise the simultaneous measurement of neural activity and behavioral state.

Behavioral state classification will use high-quality videography and novel, machine learning-based approaches for quantifying spontaneous motor output, often in the context of ongoing clinical care. Examples include pupillometry and eye tracking, heart and breathing rates, facial and body movement analysis, sleep monitoring. Data collection strategies could entail inclusion of video cameras to record behavior and facial expressions, as well as wearable devices for passive collection in ecologically salient environments. These "add-ons" to existing clinical settings would yield high volumes of rich data while minimizing resource consumption. Brain structure and neural activity will be monitored using EEG and MR-based imaging to assess the modulation of spontaneous dynamics, sensory-evoked responses, and functional connectivity as a function of behavioral state. The initial focus will be on "resting state" activity and sensitivity to visual and auditory inputs, as these are minimally burdensome to human participants and applicable across diverse model systems. Later efforts will expand to incorporate assays of emotional and motivational state and cognition. These neural, perceptual, and behavioral state data will provide a rich data set that will be heavily mined by collaborating groups (see Cluster 2).

While several Yale clinics evaluate patients with neurodevelopmental disorders across the life span, phenotyping is not standardized and few patients are genotyped. Using the existing expertise here at Yale as a framework, we will establish a cohort of subjects at Yale who are comprehensively

evaluated for a core set of standardized phenotypes and genotypes across the lifespan. All human subjects would be invited to provide tissue or saliva samples (e.g., lymphoblasts, fibroblasts) for long-term storage and sequencing (Whole Genome Sequencing and RNA sequencing, see Cluster 4) and development of stem cell models (see Cluster 3).

Cluster 2: Animal Models

Animal models of neurodevelopmental disorders are a critical paradigm for generating causal, mechanistic links between molecular and genetic perturbations and behavioral phenotypes. The goal of this Cluster is to standardize and synergize efforts across Yale laboratories working to characterize the relationships between brain activity, neural circuit architecture, and behavioral state in the context of known genetic perturbations. A variety of approaches are used to measure spontaneous and sensory-evoked activity stimuli. In mice, methods include cellular and wide-field mesoscopic calcium imaging, fMRI, and EEG, while in zebrafish, methods include whole-brain light-sheet calcium imaging. These efforts will be enhanced by cell type-specific expression of indicators, allowing detailed dissection of how various neuronal subpopulations interact in the awake, behaving animal. Moreover, these approaches can be applied to culture systems (e.g., organoids, see Cluster 3), providing direct comparisons of neural dynamics in patient-derived and animal models with the same genetic perturbation. To characterize variations in behavioral state, all studies will be combined with high resolution videography to monitor fluctuations in spontaneous motor variables, forming direct links to human studies from Cluster 1. We will combine this dissection of neurodevelopmental impact on neural circuits and behavioral state with analysis of these animal models at the genetic and molecular levels, including single-cell RNASeq.

Efforts to relate these broad classes of data (genetic, molecular, neural activity and behavioral variations) will be supported by collaborations with the Data Science resources at Yale. The broad goal is to understand similarities between human and animal model neurobehavioral phenotypes. For example, we can ask whether genetic perturbations that model our human patient populations give rise to similar neurobehavioral disjunctions, ultimately using animal models as platforms for therapeutic explorations. Collection of these large data sets across multiple species (humans, rodents, and fish) will significantly boost the ability to triangulate on mechanisms of neurodevelopmental disorders, identify potential interventions, and test therapeutics.

Cluster 3: Human iPSC and Organoid Models

The study of human-derived neurons and brain organoids, a cutting-edge strength at Yale, is critical to understanding the pathophysiology of neurodevelopmental disorders as they provide insight into human developmental states that cannot be obtained from animal models. The Yale Stem Cell Center has extensive expertise in generating iPSC lines from patients and modeling human disorders using iPSC-derived neurons and three-dimensional culture systems (e.g., organoids), although iPSC models are not currently made on a large scale. Comprehensive genomic and proteomic studies of subjects with defined genetic defects will offer opportunities to identify convergent molecular, cellular and developmental mechanisms, and to link those mechanisms to clinical behavioral phenotypes. We will generate organoids from patient iPSC lines and examine longitudinal development, transcriptomics and proteomics (see Cluster 4). In addition, we will foster collaborations with imaging and electrophysiological groups at Yale (see Cluster 2) to examine cellular function and connectivity in organoids as well as network activity. We will establish a biorepository of IPSC and brain organoids from subjects with established genotype-phenotype data that use Whole Genome Sequencing,

single- cell transcriptomics, and proteomics to generate comprehensive cellular, molecular, and genetic data.

Cluster 4: Genomics

A key goal of this initiative is to use cohort-wide analysis to examine clustering of genotypes with biologically specific phenotypes, merging studies of human patients, animal models, and stem cell-based culture systems. However, the genetic heterogeneity of neurodevelopmental disorders presents challenges to identifying specific risk-associated genes, hindering efforts to dissect disease mechanisms.

There is extensive expertise in next-generation sequencing technologies and quantitative methods here at Yale that allows genome-wide surveys of large patient cohorts to identify genes with de novo damaging mutations, providing a quantitative definition of risk and highlighting the convergence of neurodevelopmental risk genes in specific regulatory networks. However, these approaches are rarely coupled with deep phenotyping (see Cluster 1) or targeted work on underlying cellular and circuit-level mechanisms (see Clusters 2 and 3). We will engage with the Yale Center for Genomic Health and the Yale Center for Genome Analysis to carry out 'omics' studies of DNA, RNA, and proteins in iPSC-derived neurons or organoids from the Cluster 1 cohorts to identify genetic variants and differentially expressed genes. This will enable comprehensive, large scale analysis of genotype and phenotype data, revealing clinical features associated with particular genotypes within and across disorders.

Deliverables

2 Years
Generate novel analyses of existing videography and EEG data (e.g., McPartland) using machine learning-based tools (e.g., DeepLabCut) and state-dependent analysis techniques developed for rodent work (e.g., Cardin, Higley) to establish a common framework for bridging neural activity and behavioral state in humans and mice.

Establish a common framework for measuring behavioral state in zebrafish and mice (e.g., Cardin, Higley, Hoffman) that is compatible with brain-wide imaging and electrophysiology in the two model systems.

Analyze functional connectivity using existing human structural imaging and resting state and activation fMRI datasets in typical development and neuropsychiatric disorders (e.g., Blumberg) and generate quantitative comparisons with functional connectivity measures in mouse models (e.g., Cardin, Higley). Establish protocols for obtaining MR data in mice to further bridge interpretations across species.

Generate organoids from existing patient iPSC lines already in use and evaluate longitudinal alterations in developmental trajectory and transcriptomics (e.g., Park, Noonan). Establish protocols for carrying out electrophysiological and imaging studies of neuronal and network activity in cultured cells (e.g., Higley, Park).

**Establish patient registry for inclusion and retention in initial and longitudinal studies. Liaise with existing research programs/cores (e.g. YCCI), and clinical programs.

**Establish a database for storing, organizing, and distributing genomic and phenotypic data from patients and jointly analyze all available genetic data across Yale laboratories (e.g., McPartland, Fernandez, Noonan).

**Develop and submit R01-level grants to support initial efforts by teams within and across clusters.

5 Years
Expand scope to capture genotype/phenotype data from a larger population of patients, build patient community. Develop a software-based approach for searching, organizing, distributing all the different data types.
Generate synergistic human and animal datasets at the genetic, molecular, cellular, circuit, and behavioral levels for a targeted set of genetic mutations already heavily studied by multiple Yale labs (e.g., Ank3, Arid1b, Chd8, Grin2b, MeCP2, Rai1, Pogz, Pten, Shank 2, Shank3, ANK3, Trio).

Submit 2-3 Program Project Grants and/or Center Grant to NIH: NIH IDDRC center grant, Center for Autism Excellence, Center for Large-scale Functional Genomics, NIMH Cross Diagnosis Center, T32.

10 Years
Broaden scope to capture genotype/phenotype data from most neurodevelopmental disorder patients at Yale. Expand searchable data set to other sites and experimental paradigms.
Initiate a new Cluster 5: Development of Novel Therapeutics and Signature Clinical Programs

What key elements would be necessary for this proposal to be successful?

To facilitate these goals, we propose providing seed funding and infrastructure support for standardizing data collection across existing Yale laboratories. We identified four important challenges to overcome:

1. **Centralized coordination of recruitment and phenotyping.** Yale has multiple clinics serving individuals with neurodevelopmental disorders. This represents an under-utilized resource for development of a comprehensive registry to support recruitment. A research registry and designated coordinator will ensure access to participants across a broad range of investigators. This approach would facilitate integration of core phenotypic measures with minimal burden and cross-species relevance.

2. **Databasing.** Phenotype and genotype data from patients and animal and cell models need to be collected in a database accessible by both clinical and basic researchers, in a format that can be used by data scientists for data analysis and characterization. This will require a tie-in to EPIC and coordination across departments, clinicians, and research groups. YCCI could potentially coordinate data sharing.

3. **Costs.** Cluster 1 will require support of research registry coordinator, a database manager, and resources for phenotyping/genotyping. Clusters 2, 3, and 4 will require support by core facilities housed in research labs.

4. **Coordination between clinicians and basic research labs.** We will continue to have bimonthly meetings of the clinical and basic research groups working on neurodevelopmental disorders. We have identified a small set of genes and gene networks that are already the

focus of efforts across Yale groups as targets for expanded short-term effort, and these groups will continue to meet to develop grant applications. We also propose a monthly ‘Research In Progress’ talk series by faculty to share research interests and ongoing work. Identifying program coordinators or directors would facilitate these efforts.

APPENDIX D

Executive Summary of Preliminary Recommendations for Health Equity Research

Committee Members: Marcella Nunez Smith (co-chair), Saad Omer (co-chair), Andrea Barbieri, Carolyn Mazure, LaRon Nelson, Kieran O'Donnell, John Pachankis, Suzi Ruhl, Megan Smith, Emily Wang

The Committee for Research in Health Equity is charged with making specific and targeted recommendations to establish Yale School of Medicine as an institutional leader in health equity research.

The call for health equity research has increased in the last decade, with the National Institutes of Health elevating its National Center on Minority Health and Health Disparities to Institute-level status. Leading academic health centers across the country have followed suit, committing substantial investment to support health equity research at their institutions. Additionally, the ongoing COVID-19 pandemic has brought long standing health inequities to the fore, resulting in increased urgency of, and national focus on, health equity research. Yale School of Medicine has invested significantly in research focused on health equity over the past few years, but many of these efforts have been siloed. The need exists to coordinate these efforts across the School and the University, and to elevate health equity research to maintain pace with peer institutions and to become a model of excellence in this field.

We envision health equity research as a portfolio of activities across the translational research spectrum that moves beyond documenting existing group disparities in health outcomes and healthcare delivery to generating solutions through the application of novel approaches. Health equity research also identifies and highlights protective factors that are traditionally undervalued and understudied. Health equity research is grounded in rigorous research methodologies and centers on the valued contributions and engagement of diverse stakeholders across all phases of research activity. We recognize our institutional responsibility to prioritize research that is responsive to com- munities and to create dynamic structures that support a unified mission to advance health equity and justice.

As an initial response to our charge, the Committee convened to review best practices at peer institutions and to generate responses to several framing questions. The Committee identified the following preliminary recommendations, organized within two domains: 1) expanding the science of health equity research, and 2) enhancing the practice of health equity in all research. The Committee will iterate on these recommendations as the perspectives of additional stakeholders are integrated. The newly created Office for Health Equity Research, with guidance from formal institutional and community advisors, will be accountable for ensuring final recommendations are incorporated into its strategic plan and will oversee implementation.

Domain 1: Expanding the science of health equity research

The first domain of recommendations concerns investing in the expertise and infrastructure necessary to establish Yale as a leader in the science of health equity research. This includes the following preliminary elements:

Establish a Fund for Health Equity Research Development: The Committee recommends that a continuous annual line-item budget allocation establish an internal fund to provide support for health equity research planning grants, pilot research grants, and bridge funding for established health equity projects. The Fund will be open to all School faculty and will prioritize support for collaborative partnerships between individuals and teams working across different disciplines and at the inter- sections of health equity research.

Develop a Shared Services Methodological Core: The Committee identified the need to support a School-wide resource focused on the methodologies commonly employed in health equity research. The Core will provide consultation in health equity research methods and approaches to investigators across the entire Yale community. The Core will build upon existing areas of strength, including community and stakeholder engagement, and will deepen collaborations with existing health equity research hubs of excellence across the University.

Recruit Health Equity Research Faculty and Staff: The Committee recommends a systematic cataloguing of ongoing health equity research at the School and University to inform a targeted and comprehensive plan to recruit emerging and established health equity research faculty and staff with complimentary skills and expertise. Recruitment of health equity researchers must be deliberate and incentives must be offered to bring these researchers to campus. The Committee recommends the recruitment plan delineate specific resources and opportunities needed to attract high caliber researchers in this field.

Incentivize Health Equity Research in Faculty Recruitment across Disciplines: The Committee recommends centralized funds be earmarked to contribute to the recruitment of faculty across the translational research spectrum whose portfolios include health equity research projects. Increasing the consideration of health equity in all faculty recruitment efforts across the School of Medicine is a key strategy to broadening the scope of health equity research at Yale. Additionally, the Committee recommends providing funds as substantial bonuses in merit increases based on annual evaluations for those who participate in health equity research and/or recruitment and retention of health equity faculty.

Improve Data Collection for Health Equity Research: The Committee recommends the development of institutional data standards for health equity research. Continued partner- ship with Yale New Haven Health System on the systematic collection and tracking of health equity relevant data is a priority. In addition, the Committee recommends the dedicated creation and maintenance of a health equity research data and variable standards resource to provide guidance for investigators across the University.

Domain 2: Enhancing the practice of health equity in all research

The second domain of recommendations concerns shifting the overall research and learning environment to assure the success and sustainability of health equity research initiatives at Yale. This includes the following preliminary elements:

Optimize Institutional Policies: The Committee recommends institutional policies be reviewed and recommendations be made for revisions as needed in order to create processes that advance equity broadly within the School. This includes, but is not limited to, policies related to faculty/ staff diversity, equitable opportunities for professional advancement, fair hiring and compensation processes, community stakeholder research review processes, and the reimbursement and hiring of community partners. The Committee recommends an institutional audit of the School community to assess knowledge, behaviors, attitudes, and expectations related to health equity research.

Promote Health Equity Education and Training: The Committee recommends the development of educational and training opportunities dedicated to health equity research for students, residents, postdoctoral fellows, as well as for junior and mid-career faculty. Additional investments in health equity research pipeline programs and experiences should be made, with a focus on providing exposure and opportunity for the next generation of investigators from New Haven and the region.

APPENDIX E

Technology Development and Biomedical Engineering – Executive Summary

Committee Members: Noah Palm (co-chair), Erica S. Spatz, (co-chair), W. Mark Saltzman, Rong Fan, Kathryn Miller-Jensen, Chenxiang Lin

GOAL
To develop a world-class, technology-focused institute, NextGen@YaleMed, that facilitates and accelerates growth in the development, scaling, and democratization of biomedical technologies, data science, and advanced analytic tools.

CORE CONCEPTS
1. Foster a culture of collaboration and open data science among Yale investigators, especially between clinical/biological departments and basic science/engineering departments by creating a world-class data lake for the sharing and adoption of big data, new technologies, and computational tools.
2. Recruit a world-class core of highly trained, technology-focused scholars in biomedical technology, data science, and medical devices with the goal of accelerating the adoption of cutting-edge technologies and analysis, iterative design, and technology innovation
3. Develop, scale, and democratize cutting-edge 'in house' technologies

USE CASES
1. SARS-CoV2 saliva test developed at Yale but scaled at the Broad Institute
2. Single-cell RNA-seq data generation and analysis still not standard or centralized w/in Yale, restricting sharing of data and collaboration
3. YCGA (and other Cores) are critical, but are not designed to be nimble (e.g., experiment with emerging technologies, support incubator ideas)

EXEMPLARS
1. Broad Institute – rapid adoption of new technologies, scale quickly in areas of focus
2. UC Irvine – data sharing/donation; supportive analytics
3. Whitehead (MIT), Sandler Fellows (UCSF), Wyss Institute (Harvard) – recruit promising young investigators; highly trained technology-focused fellows

STRATEGIC VISION: To develop NextGen@YaleMed with 3 interconnected and synergistic pillars

1. NextGenConnect@YaleMed – centralized hub and social network for data and protocol sharing and scientific matchmaking (open only to Yale investigators); works closely with Yale USSC data science initiatives and scientific cores
    a. Methods for secure movement and facile data sharing (locally and publicly)
    b. Data cleaning and aggregation (standardization; common data fields)
    c. Integration of tools and computational algorithms
    d. Social network that fosters collaboration (e.g., data links to individual/lab profiles, protocols)
    e. Creates mechanism for Yale community to decide which new tools/technologies to invest in/adopt (e.g., at Yale cores)

f. Reduces barriers for trainees to incorporate new techniques/technologies into their work

2. NextGenFellows@YaleMed – a world-class fellowship program to bridge technology, biology, medicine, and data science
    a. Recruits highly talented, technology-focused research scientists from across the world. Fellows will bring new technologies, iterate ideas, and accelerate collaborations.
    b. Three tracks: technology development, medical devices, and data science
    c. Fellows are co-located in an open and flexible lab/office environment adjacent to Data Science and the NextGen Technology Incubator to encourage cross-disciplinary collisions
    d. Fellows are matched with Yale labs for 1-2 years so they become embedded in a team
    e. Potential for retention as faculty or permanent staff
    f. Cohorting of fellows facilitates cross-pollination and innovation; fosters lasting connections across disciplines; nucleates a unique and expanding network of NextGen@YaleMed scholars

3. NextGenTech@YaleMed – a technology incubator to test, scale, democratize and commercialize priority cutting-edge technologies
    a. Centralized space for testing new ideas and scaling mature technologies beyond their home laboratories (CLIA certified?)
    b. Staffed by 'super technicians' and innovation junkies
    c. Competitive process for resources to test, refine, validate, and optimize Yale technologies
    d. OCR and CHI representatives embedded within the incubator to facilitate technology transfer and commercialization (integration of Blavatnik Fellows or OCR/CHI staff)
    e. Successful technologies graduate to biotech incubator space

NEXT STEPS/TIMELINE:

4. Begin recruitment of Executive Team – start immediately

5. Establish NextGenConnect@YaleMed – start now, target launch date: 2021
    a. Design in collaboration with Yale labs, Cores & end-users (trainees); integrate with Data Science
    b. Beta versions - test and iterate with key Yale labs

6. Inaugurate NextGenFellows@YaleMed – create vision; recruit inaugural class for 2022
    a. Establish faculty committee to lead recruitment of inaugural class of fellows (2021)
    b. Identify core and affiliate faculty; new BME faculty in 100 college would affiliate as core faculty
    c. Advertise/recruit fellows for July 2022 start

7. Develop NextGenTech@YaleMed – target ribbon-cutting 2022
    a. Start with areas ripe for impact/application – work with new leadership team; design with NextGenFellows@YaleMed in mind; nurture 2-3 novel/untested ideas for pilot projects; select 2-3 mature technologies ready for scaling
        i. Coordinate with Cores (Janie Merkel)
        ii. Engage/coordinate with OCR (Jon Soderstrom) and CHI (Malgorzata Cartiera)
    b. Establish Development Committee

i. Identify donors (? Blavatnik, Tsai)
ii. Secure space adjacent to start-up incubator at 101 College St

APPENDIX F

Strategic Planning Committee on Biomedical and Biological Imaging at Yale Executive Summary

Committee Members: Joerg Bewersdorf, (co-chair), Gigi Galiana, (co-chair), Henk De Feyter, Shawn Ferguson, Carolyn Fredericks, Jaime Grutzendler, Chi Liu, Graeme Mason, Walther Mothes, Xenophon Papademetris, Dana Peters, Katerina Politi, Hesper Rego, Dustin Scheinost, Richard Torres, Yong Xiong

Additional consultations with: Al Sinusas (Cardiology), Preston Sprenkle (Urology), Jim Duncan (Biomed. Eng., Electrical Engineering, Radiol. & Biomed. Imaging)

Process of Discussion

The committee met three times in August, and members reviewed this summary of the discussion. Additional stakeholders were consulted individually. Despite the wide range of faculty consulted, the committee discovered a surprisingly strong consensus in the themes identified, reflected in the presented recommendations below.

Importance of Imaging at YSM

Imaging is required for discoveries in nearly every field of biomedical research represented at YSM, and it is a key connection point for collaborations across disciplines and departments. While this is true of imaging as a field in general, the programs at YSM are especially high impact, enabling tomorrow's biomedical research around the world.

YSM is already a national leader in imaging research: Pioneering work has been and is performed in light and electron microscopy, MRI, MRS, PET and image analysis, reflected for example in 20+ seminal papers with >1000 citations. Putting this in a national context, YSM Radiology, representing a subset of Yale imaging, ranks #5 in NIH funding nationwide (BRI, 2019).

Imaging at YSM is diverse, ranging from whole-body to Angstrom resolution and from instrumentation and algorithm development to applications. This diversity is reflected in a heterogeneous institutional structure including large laterally integrated centers, like the MRRC, smaller imaging facility cores as well as many individuals distributed across the majority of YSM departments.

Unrealized Opportunities in YSM Imaging

Three major topics emerged from the committee's discussion:

Collaboration beyond local networks: The YSM imaging community is collaborative by nature, but individuals lack an overview of the institutional landscape because of its complexity and size. It is therefore difficult for users to understand what is available, either via fees, collaboration, or through training. Coordination with the hospital was also cited as a challenge for translational projects.

Program grants and training grants: The committee expressed strong enthusiasm for both training and large program grants, but the high administrative burden and the need to prioritize their individual labs

was a hindrance to engage in these community services. Better coordination of these efforts and administrative support could facilitate these grants.

Services and support personnel: Increased research scientist staff support to properly acquire and analyze images would significantly enhance the quality of imaging-based research results. Departments or individual groups that might provide new services are currently, however, discouraged by the long-term responsibility to support this staff and maintain the service. These and other common needs, both material (data storage) and political (coordination with hospital), could be addressed more efficiently with central coordination.

Committee Recommendations

In response to these unrealized opportunities, the committee recommends:

Engagement of YSM in interdisciplinary collaborative activities: Seminars, workshops and networking would provide guidance and momentum for large-scale grants. Educational programs and training grants for disease-specific imaging (e.g. neuro or immunobiology) are seen to be clearly within range. Imaging-targeted pilot funds to incentivize biomedical researchers to explore whether a particular imaging modality would be a match for their research question could in particular benefit YSM individuals outside the existing imaging networks or imaging-centered departments.

Centrally supported infrastructure: Hiring an Imaging Liaison would provide a hub that connects and coordinates people within and beyond the YSM imaging community. Midlevel research scientists could assist and educate non-expert users in acquiring and especially in processing imaging data. Additional infrastructure for data storage and computing needs would support the larger imaging community at YSM.

Proposal to Implement Recommendations

These recommendations could be realized by the formation of an **Interdepartmental Bioimaging Center**. As each existing imaging-focused entity at YSM, whether it is a large core facility or an individual lab, has had significant success independently, an overarching center should not compromise the current level of autonomy. However, an umbrella imaging center could simultaneously address all committee recommendations by acting as a hub of information, as well as a home for central staff, infrastructure and programs. In addition to addressing the recommendations above, the committee identified many further benefits such a centrally supported imaging center would offer:

- Encouraging innovation by fostering interactions across techniques, scales and anatomy
- Enhance the productivity and recruitment of faculty doing imaging work outside imaging-centric departments
- Facilitate more research opportunities for clinicians
- Branding of a recognizable center would increase visibility of YSM as a major national center for imaging
- Will bring in grants and donors to support the imaging infrastructure (service and research)
- Support recruitment to address underserved research topics in YSM imaging, such as: quantitative analysis of microscopy data (incl. AI), CT imaging, ultrasound imaging, and chemical probes for optical and medical imaging

Deliverables and Timeline

While other universities have renowned imaging centers at either the medical or cellular scale, we see the unique opportunity to establish YSM as a center for imaging that unifies strengths *across all scales.* This would be a powerful differentiator to solidify Yale's leadership in bioimaging.

Goals:

Year 1	Interdepartmental Bioimaging Center inaugurated
	Administrative Director hired (acting as liaison and grant support)
	1 Research Scientist hired to support YSM researchers in image analysis
Year 2	Network of 20+ imaging-focused labs from 8+ (basic & clinical) YSM departments formed
	Seminar series and workshops established
	2 imaging-focused faculty hired to bridge gaps
Year 3	Network expanded to 30+ imaging-focused labs from 12+ YSM departments
	1 training grant (T32 or similar) on bioimaging funded
	1 bioimaging-centered P41 (or similar) grant funded
	1 more Research Scientist and 1 more administrative support staff hired (paid by grants)
Year 4	International reputation as center of innovation for bioimaging technology development and application established
	Endowment secured
	2 more imaging-focused faculty hired
	Outreach towards more translational research and commercialization efforts

APPENDIX G

YSM Strategic Planning in Translational Medicine Working Group

Committee Members: Mustafa K. Khokha (co-chair), Uma Reddy (co-chair). David N. Assis, Charles Dela Cruz, Cary Gross, Peter Gruber, Jeanne Hendrickson, Monique Hinchcliff, Jonathan Leventhal, Serena Spudich, Miriam Treggiari, F. Perry Wilson

Definition: Translational medicine can be viewed broadly and encompasses much of biomedical science. For the purposes of this Working Group, we operationalized translational medicine as research "inspired by patients, for patients." In this way, translational medicine can be both basic and clinical science but is patient- centric and timely as to inform our understanding of the disease process or therapeutic options. Importantly, in addition to basic and clinical sciences that lie at the bench and bedside (T0-T2 translation), translational medicine *must* also incorporate real world care and outcomes (T3 translation) and community and population health (T4 translation).

NCATS definition of Translational Research: The process of turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public — from diagnostics and therapeutics to medical procedures and behavioral changes.

The Working Group was charged with the following questions:

- Are there models for excellence in this field? What is it that makes them successful?
- Is this an area that would require faculty recruitment to significantly move forward? What scientific "holes" would recruitment focus on? Would faculty recruitment include senior leadership recruitment (that is, an external and potentially internal search)
- To move forward, are there needs for specific equipment-based core facilities that are not currently available at Yale
- Is there a "service component" that is needed to pursue this area, that is, core facilities staffed by experts that provide fee-for-service consultation? If so, what are the specific needs that would support and develop extramurally funded support?
- What "large grant" (P01, U54, etc) funding mechanisms are appropriate to enhance and sustain this area? What Departments/Schools need to work together to obtain significant large grant extramural support?
- Is this an area appropriate for a training grant? If not, why not? Do we have faculty who can pursue a training grant?
- Is co-localization of the faculty an important part of enhancing this area? If so, please identify core faculty currently at Yale who would be willing to give up their current locations.
- What would success of an enhancement plan in this field look like?

Overall Assessment: Translational medicine at Yale has been productive despite insufficient infrastructure by YSM and YNHH. At YSM/YNHH, translational medicine is a grass roots effort driven by the creativity, innovation, and determination of individual, experienced investigators. Importantly, early-stage investigators or investigators new to translational research face what seem like insurmountable barriers to translational research. YSM/YNHH is being eclipsed by comparable institutions in translational research. Without significant improvements in the translational research infrastructure, the Working Group felt strongly that our competitive disadvantage will only worsen as other institutions move forward.

Overall Recommendation: A coordinated effort between YSM and YNHH is essential to successfully support translational medicine, benefitting both institutions. YSM will advance a major mission of the medical school as well as attract the best clinicians, physician-scientists, and basic scientists. In

addition, YNHH will benefit by attracting patients who view hospitals with cutting edge research and therapeutics as the best. Success in translational medicine enhances the reputation of the hospital, and hospitals listed at the top of the US News and World Report are those with tremendous translational research infrastructure. Critically, improving translational medicine at Yale requires careful study, and while the Working Group identified many issues that need to be addressed, we all agreed that a thorough assessment and plan is necessary that will take more time than the brief meetings held by this Working Group. Below, the Working Group identified some of the major issues but is far from complete. Overall, the Working Group recommends that senior leadership at YSM and YNHH, together, either extend the efforts of the current Working Group or create another Working Group to 1) comprehensively define the scope of translational research at Yale, 2) evaluate research productivity over time compared to comparable institutions, and 3) identify the necessary infrastructure needed to improve translational medicine at Yale.

Issues in Translational Medicine at Yale:

Bridges between Basic Science, the Clinic, and Populations

A critical component of translational research is bridging between the clinic and the bench. While Yale is remarkably collaborative both across Departments and across Schools (including Public Health and Nursing), the ties between clinicians and basic scientists within and between these Schools needs to be enhanced.

There are many potential reasons for this: 1) efforts to increase clinical productivity leave little time for academic pursuits or opportunity for research collaborations; 2) clinicians are de-incentivized to participate in research activities as collaborative (middle) authorship is little valued at YSM/Departments; 3) there is growing tension between the clinical and basic science departments based on the perception that clinical revenue supports researchers in basic science departments but not in clinical departments; and 4) a relative paucity of infrastructure dedicated to the support of T0-T4 research, including centralized clinical and administrative data and biospecimen repositories, robust statistical support, IT/informatics support, and resources to assist investigators interested in translational research.

Training, Recruiting, and Retaining Physician-Scientists

At its core, physician-scientists are fundamental to translational research. Physician-scientists can dramatically improve communication/collaborations between basic scientists, clinicians, and population health experts. However, physician-scientists are under fire at all levels. As trainees, the marked increase in competition for trainee awards (K08, K23) means that many potential physician-scientists are lost for lack of training support. As independent investigators, the combined demands of maintaining brisk clinical productivity and NIH-supported, protected, research time are becoming more and more difficult to meet. In fact, the lack of support for protected time for physician-scientists has made Yale unattractive for many making it difficult to recruit and retain. In order to be successful at translational medicine, supporting physician scientists at all levels is essential.

Clinicians and Clinical Educators

Both basic scientists and physician-scientists need clinicians and clinical educators to be incentivized to contribute to translational research. Many clinicians choose academic settings because translational research enriches their clinical practice. However, the heavy productivity demands are eliminating the needed time to engage in translational research. Therefore, additional incentives are essential to keep clinicians engaged in translational research. For example, the acknowledgement of middle authorship on translational studies in promotion decisions. In the case of grants, multi-PI grants with clinicians should recognize the efforts of clinical departments. Rather than indirect costs

being distributed only to the contact PI, these indirect costs could be distributed to other departments including the clinical departments contributing to the grant.

Infrastructure for Research

- Need to expand the role of YCCI to be able to better support researchers at all levels. YCCI can be useful to early-stage investigators/trainees to get started in their research program. However, YCCI does not scale or have capacity to support the translational mission across all researchers. We need a translational infrastructure that is investigator-centric and operationally more pro-active rather than administrative. One possibility would be to create an **Institute for Translational Medicine** that would identify faculty across Departments and could facilitate interactions and support (an umbrella structure that incorporates YCCI). Alternatively, Yale could expand the reach of YCCI (a hub and spoke structure).
- Establish comprehensive research infrastructure across all YNHH hospitals and community care locations to ensure subject recruitment including:
    - Single IRB
    - System for screening patients that fulfill study inclusion criteria across YNHH and community care locations
    - Method to collect and transport study participant biospecimens back to Yale
    - Develop a clinical coordinator pool whereby clinical coordinators cross-cover each other to avoid delays/interruptions in subject recruitment
- Need core labs to perform research tests plus improve the process for research laboratory testing to be conducted in hospital labs. Hospital labs are understaffed and the protocol for coordinating research laboratory testing and for obtaining research pricing is a major barrier for investigators (needs streamlining).
- Need stronger informatics core and IT support. More support for JDAT is essential to be able to get timely and reliable data, also implementing and evaluating EPIC-based interventions, wearable technologies, etc. In addition, bioinformatics cores to analyze sequencing data.
- FISMA moderate security environment needs to be fully supported by Yale University and YNHHS as it is required for an increasing number of grants and contracts.
- Patient-Voice Core: Personnel and resources to assist investigators with the selection, implementation, and interpretation of patient-reported outcomes (PRO) instruments, qualitative research methods, and support for selection, creation of psychometrically sound survey tools.
- Yale needs to be able to serve as the single IRB for multi-site studies being led by Yale investigators. Single IRB is required for NIH funded studies. Because Yale cannot serve as a single IRB, Yale investigators are at a disadvantage when applying for NIH grants compared to our sister institutions. Yale investigators need to pay for external IRB reviews which are costly and not in keeping with the expected resources with an institution such as Yale.

Research Funding

More and more, translational aspects of research are necessary to secure funding. To that end, enhancing the infrastructure for translational medicine at all levels will make a major difference. This can facilitate collaborative grants between researchers in basic and clinical departments, across Schools (YSM, Yale College, Public Health, Nursing) and as well as within departments. In addition, large grants are only possible when the necessary translational research infrastructure are present and functioning effectively. Importantly, for the future of translational medicine at Yale, philanthropy is essential. **Yale must diversify and expand its funding portfolio if we are to be competitive with our sister institutions**. The lack of philanthropy and endowment supporting translational research at Yale leaves investigators at a serious disadvantage compared to our peers. Of note, while donors are interested in impactful research, they are particularly inspired by the impact on patients and the

transformation of their lives; therefore, translational research is particularly well suited for philanthropic support and should be a specific focus.

Space

Space at Yale is at such a premium that it inhibits research endeavors. There is a shortage of space for basic research labs and cores as well as little to no space to recruit patients into clinical studies. As an example of the impact on translational research, many institutions including UConn have incubator space where startup companies can grow in order to develop the next generation of patient therapeutics. Quality in-hospital and outpatient clinical and research space is essential. This was highlighted by the recent COVID-19 related study efforts.

Identity

A major challenge for translational research at Yale is that it is compartmentalized across many different departments in part due to its "grass roots" structure. Consequently, in both clinical and basic science departments, there is a lack of understanding as to who is doing translational medicine and a relative paucity of interaction between translational researchers. As such, it can be difficult for young investigators to find mentorship or established investigators to develop collaborations that can and should exploit the talent of researchers across YSM/YNHH. The formation of an Institute of Translational Medicine could create the necessary structure for a collaborative environment across translational medicine. We note that many of our sister institutions (**Stanford** Bio-X, **Harvard** Catalyst, **Vanderbilt** VICTR, **Hopkins** ICTR, **Penn** ITMAT, and many others) are far ahead of Yale in developing such collaborative structure.

Recommendations:

- YSM/YNHH together work to continue this Committee and broaden/change membership to include YCCI and other critical stakeholders to enlarge the scope and ensure translational research remains a major focus for YSM/YNHH

- Obtain baseline metrics by conducting an in-depth analysis of how much translational medicine is currently conducted, who is doing it, and where it is being conducted
- \Specifically perform an in-depth analysis of the existing research Cores at YSM dedicated to translational research to better understand how well they are fulfilling the mission of promoting research (i.e. how user-friendly, how affordable, and how well they are advertising their services to the YSM community)

- Evaluate the barriers for physician-scientists, clinicians, and basic scientists to engage in translational research holistically including training and development of these investigators, barriers to participation, as well as challenges for funding

- Study models for excellence in this field such as institutions like Vanderbilt, Stanford, Harvard, Duke, Penn, and Johns Hopkins among many others

- Recruit senior and early career physician scientists particularly from underrepresented groups that are interested in performing translational research and nucleating or participating in team science.

- Improve informatics infrastructure and access to investigators + reconfigure JDAT to a more comprehensive resource that can focus on the needs of translational researchers

- Bolster YCAS to ensure that investigators with a focus on translational research have access to biostatisticians with diverse expertise.

- Establish core research laboratories and improve and expand research space. Larger funding mechanisms (P01 or U54 grants) submitted by mid-career or senior faculty could support core facilities to enable translational research. Administrative assistance to support, submit, and maintain these large grants is essential and could be a thrust of an Institute of Translational Medicine.

- Establish multi-disciplinary training programs (K12 and T32) in translational research. For example, we could establish training programs across clinical departments to train clinical research fellows in basic science labs. Alternatively, we can create training programs where PhD students and postdocs with basic research training are placed in translational research labs in clinical departments. Training programs could bridge schools (for example, YSM clinical departments with interest in community health and the School of Public Health). Administrative assistance to support, submit, and maintain these large grants is essential and could be a thrust of an Institute of Translational Medicine. Importantly, for clinical research fellows, we need mechanisms to support salaries over the NIH limits (T32).

- Establish "Patient Voice Core" to ensure that investigators have expertise and support for efforts to incorporate patient reported outcomes and quality of life measures

- Further investment to support Community-Based Participatory Research (CBPR) including the recruitment and engagement of faculty who can build trust and alliances with the community so that patient-based research studies are perceived as an investment in the community rather than community-based experimentation.

- Diversify translational funding. Engage the Yale Development Office to aggressively engage philanthropy and industry to support translational research. The reliance on NIH funding alone will leave us further and further behind our sister institutions. Establish active, dedicated campaigns to raise large amounts of funding ($100 million, $1billion) to establish an Institute of Translational Medicine. Leverage the Yale brand to focus fund raising efforts for research from individuals and industry

- Establish an Institute of Translational Medicine, a formal collaboration between YSM and YNHH, to provide central coordination of research and mentorship by successful senior faculty of junior translational medicine faculty. Create a physical space (building) for core investigators to foster
- collaborative, interdisciplinary research. The Institute would hold joint seminars and brainstorming sessions for collaborative grants/projects.

- Committee meetings with YSM and Hospital leadership to present recommendations to encourage alliance and cement commitment towards translational medicine research. Now is an exciting time as we have a new Dean of YSM and a new President of YNHH.

APPENDIX H

Clinical Trials Strategic Planning Committee -- Executive Summary

Committee Members: Miriam Treggiari (co-chair), Stuart Weinzimer (co-chair), Steven Bernstein, Onyema Ogbuagu, Stephanie O'Malley, Daniel Petrylak, Uma Reddy, Gerard Sanacora, Eugene Shapiro, Eric Velazquez

Our vision: The Yale Center for Clinical Trials Research
This Center will provide a full array of clinical research services essential for the conduct of clinical trials and will interact with other allied organizations within the University, bridging translational research and implementation science. It will oversee all regulatory and compliance aspects of clinical trial conduct at Yale, ensuring institution-wide standards and serve an important educational and incubator function, facilitating the mentoring, training, and collaboration of investigators within the institution

Our existing strengths and resources:
Yale is already home to many different groups conducting cutting-edge research and has many institutional resources devoted to the research mission. We have ample senior-level investigators to provide mentoring and an elite clinical care network with access to patients in CT, NY, RI, and MA, which can be leveraged to further our research mission.

Our existing challenges:

- Infrastructure: Our clinical trials resources, while ample, can be difficult to access and manage with efficiency, particularly our contracting and budgeting process. Our trials data management systems need to interface more smoothly with our EHR, and our IRB is not currently empowered to oversee multi-center trials with Yale as lead site.
- Compliance: There is currently insufficient oversight of study conduct and compliance with federal regulations and a lack of central coordination. Many of these functions exist already within the YCCI, but these services are underutilized and are not applied across the institution.
- Networking: It is difficult for the research community to connect with each other and challenging for early-career investigators to find mentoring. Further, there is insufficient dedicated financial support for mentoring, in the form of start-up funds for early-career investigators and protected time for mentoring.

Recommendations to achieve our vision of a Yale Center for Clinical Trials:

1. **Infrastructure**
   - Centralize and organize all contracting, budgeting, regulatory, and compliance functionality within the Center. Internal review of budgets and contracts will accelerate study approvals and prevent Yale from missing opportunities with very tight timelines. An enhanced study "dashboard" will allow all involved personnel rapid access and communication and improve study tracking and project management.
   - Empower the Center with Integrated, comprehensive compliance oversight of clinical trials to assure that all studies are conducted with the highest standards of good clinical practice and mitigate risk to investigators and the institution. The Center will assist investigators in developing their own standard operating procedures, liaison with FDA, clinicaltrials.gov, and other federal regulatory bodies, and support Yale IRB to serve as IRB of record for multi-

center trials.
- Create a unified, automated, and FDA-compliant data management systems to provide seamless communication with the EHR and other institutional databases and Yale ITS and enable a secure single server to receive and store multi-center data.

2. Faculty Development
- Develop training programs specifically designed for clinical trials research, including formal didactic content on scientific and administrative aspects of conducting clinical trials; a core of senior faculty to foster mentor/mentee relationships and review grants and projects; and start-up funds for early-career investigators and protected time for senior faculty mentors.
- Strengthen inter-disciplinary connections and collaborations by designating clinical trials leads within departments, establishing online portals to facilitate collaborations and promote existing research foci; and implementing other communications strategies (seminars, retreats) to foster connection.

3. Paradigm Shifts
- Invest more hospital support and value for clinical trials research: appreciation that cutting-edge clinical trials research attracts providers and patients and promote philosophy that every patient is a potential research participant
- Expand geographic footprint of research services: leverage our existing network of hospitals and other outpatient ambulatory centers to serve as research facilities. This "hub and spoke" model will improve patient access to research trials and enable greater diversity in enrollment. We can accomplish this with greater sharing of services and greater utilization of telehealth for research
- Commit to building the Yale "brand" for clinical trials research. We can advance our reputation as an partner of choice for clinical trials by improving our efficiencies in contracting/budgeting and meeting recruitment targets and study milestones. By investing in clinical trials research as an academic endeavor with dedicated funding, support for early-career investigators and senior mentors, and recognition for academic advancement, we can attract and retain elite clinical investigators

4. Action Items, Metrics, and Timelines
- Baseline assessment of the current status of clinical trials research at Yale, including a database of current studies, a roster of potential faculty leads in each department engaged in clinical trials research, and an analysis of the time required for studies to move through the contracting, budgeting, and regulatory approvals process. We also need to conduct a needs assessment to identify requirements for network hospitals and ambulatory centers to serve as clinical satellite sites.
- Expansion of infrastructure to include maintaining a repository of all existing clinical trials research at Yale; enhancing online navigational tools for tracking of trial status at all stages; building a reliable billing system for all research-related charges, especially on hospital side; growing the mentoring programs for both the scientific and administrative aspects of conducting clinical trials
- Success criteria will include: increasing total number of new submissions, new awards, and success rate; accelerating the pace of approvals process from receipt of materials to approvals of contracts and budgets; building our reputation, through increased selection of Yale as site, meeting recruitment and timeline goals; and scores on faculty satisfaction surveys; and increasing recruitment and retention of faculty engaged in clinical trials

research.

- 5-year goal: Meet infrastructure goals to better serve the existing institutional efforts, build foundation for growth, and enhance our reputation
- 10-year goal: With track record of successful and efficient research enterprise in place, we can successfully compete for program and center grants

Respectfully submitted,
Stuart A Weinzimer, MD and Miriam Treggiari, MD, PhD, MPH On behalf of the Clinical Trials Working Group

APPENDIX I

Fostering Research Collaborations Across Disciplines

Committee Members: Stephanie O'Malley (co-chair), Ed Kaftan (co-chair), Paul Aronson, Jeanne Hendrickson, Nik Joshi, Sam Katz, Kasia Lipska, Ruth Montgomery, Lauren Sansing, Wade Schulz, Robin Whittemore

DEFINING SCOPE: WHAT IS INTERDISCIPLINARY RESEARCH?

Interdisciplinary research is any study or group of studies undertaken by scholars from two or more distinct scientific disciplines. The research is based upon a conceptual model that links or integrates theoretical frameworks from those disciplines, uses study design and methodology that not limited to any one field, and requires the use of perspectives and skills of the involved disciplines throughout multiple phases of the research process. The committee views "disciplines" in a broad sense and includes traditional scientific disciplines (e.g., pediatrics, psychiatry, pharmacology, chemistry, cell biology, genetics, nursing), domains (e.g., addiction, cancer, inflammation), conceptual ideas (e.g., social justice, health disparities) and methodological approaches (e.g., neuroimaging, clinical trials, implementation science).

WHY SHOULD INTERDISCIPLINARY RESEARCH BE AN AREA OF EMPHASIS?

- To solve complex problems that are not going to answered working from a single perspective.
- Collaboration with others outside your expertise can help you develop another skill set that can enhance your ability to contribute meaningful to different projects in different domains.
- A powerful motivator for junior investigators who want to grow their science beyond what an individual investigator can do.
- Improving the research enterprise can lead to increased grant funding.
- More ambitious projects generate enthusiasm and support fund raising.
- It's fun! (May reduce burnout)

BARRIERS and SOLUTIONS:

- Faculty do not know the breadth of potential collaborators at Yale. Need a means to connect people and increase the likelihood of scientific "collisions" that may lead to collaborations.
  - AI solutions: (e.g., Harvard Catalyst profiles)
  - Matchmakers/Champions: Individuals in departments/schools who know the breadth of potential collaborators and who can make introductions as well. Champions should have a means/forum to link to each other.
  - Invite speakers to departmental symposia from other Yale departments/schools

- Siloed culture at Yale
  - Helping people feel welcomed and that others are approachable.
  - Requires leaders invested in making sure that there is a broad collaborative group and that includes everyone in some way. For large grants, requires a PI or senior leadership to identify and bring along the interested junior faculty and make sure they understand what's expected and can succeed in their role.

- Concerns about whether team science is valued in the faculty promotion process

- Interdisciplinary team science is considered in promotions on the Investigator track but may need to be addressed in other tracks as well. While there remains a need to excel in an area, uniquely contributing to interdisciplinary/team science should count
- Individual contributions to interdisciplinary science as well as the effort of faculty to promote and mentor others in interdisciplinary research should be valued.

- <u>Inadequate infrastructure and support for interdisciplinary research</u>

  - Establish the vision for interdisciplinary thinking and research at Yale
    - Conduct a Dean's Workshop to share the vision of interdisciplinary research at Yale and serve as a kick-off to new interdisciplinary initiatives
      - External speakers (e.g., Koch Institute) about practical considerations
      - Internal speakers who have done this well
    - Expand this approach to host ½ -2day meetings, with selected talks and break out groups
      - Jointly organized across at least 2 different departments/schools.
      - Could focus on provocative questions or a timely topic where interdisciplinary work could advance research (e.g., CoReCT group's RFA for COVID-related interdisciplinary pilot grants)
      - Follow-up, action-oriented meetings (might lead into pilot applications)
      - Students in the labs could generate topics/speakers

  - Establish Center for facilitating interdisciplinary research
    - Administer pilot funding for promoting interdisciplinary research collaborations
      - Would operate like NIH's cooperative agreement model (U-type) – a partnership between the Center and interdisciplinary research teams.
      - Establish evidence of collaboration and generate preliminary data needed for extramural funding mechanisms
    - Provide support for awarded collaborations
      - Dedicated program/project manager to help coordinate and track progress
      - Provide expertise in pre- and post-award grant process
      - Discretionary-type funds to contract medical writers, editors and graphic specialists on an as-needed basis

  - Leverage existing investments in data science
    - Access to diverse datasets can be a powerful nucleator of interdisciplinary thinking and research
    - An Example: The Computational Health Platform (CHP), although still under development, was the nucleus of a large interdisciplinary team formed in response
    - to COVID-19 and resulted in numerous interdisciplinary publications and grant applications, including P30 and P50 supplements, a U54 among many others.
    - A portion of the pilot funds administered through the Center (described above) should be dedicated to interdisciplinary teams utilizing such datasets

EXISTING ASSETS AT YALE

- Exceptional depth and breadth of faculty expertise and institutional resources
- Existing examples of large initiatives engaged in interdisciplinary research (see examples at

the end of report)
- Existing training grants engaged in interdisciplinary training that can serve as a pipeline of new investigators (see examples at the end of this report
- Institutional experience led by Carolyn Mazure adapting the Investigator Track to incorporate interdisciplinary science (definition of interdisciplinary science and operationalization of how an individual contributed uniquely to team science)

DELIVERABLES and TIMETABLE

- Promote value of interdisciplinary research
  - Plan Dean's Symposium to foster interdisciplinary thinking and collaboration – Act as a "kick-off" to initiatives (Year 1, hold year 2)
  - Annual symposiums as follow up from prior year (ongoing)
- Improve ability to identify collaborators
  - Adopt Harvard's Catalyst Profiles to help connect researchers from diverse disciplines and fields (Year 1)
  - Identify champions/designated people to connect faculty to collaborators or mentors outside the Department (Year 1)
- Provide infrastructure to support interdisciplinary research
  - Establish a Center that supports interdisciplinary research, including pilot funding (Years 1-2)
  - Nucleate interdisciplinary research teams (Year 2 and beyond)
- Evaluate and revise Faculty Tracks and materials to recognize the contributions of interdisciplinary scientists to research
  - With the background developed through revision of the Investigator Track (e.g., agreed upon definitions of interdisciplinary research and how it is operationalized), identify committee members and a committed leader with expertise in interdisciplinary science and knowledge of school-based faculty guidelines and committee members (Year 1) and initiate the process.
  - Finalize and seek approval for revised documents (Year 2-3)

MEASURES OF SUCCESS

- Increase in number of grant submissions with interdisciplinary representation
  - mPI R01; U, P type; foundation grants
- Increase in diversity of investigators on these applications
  - across disciplines, departments and schools
- Increase in success rate and funding levels

EXAMPLES OF INTERDISCIPLINARY EFFORTS AT YALE (not an exhaustive list)

- Yale Institute for Global Health and the Global Health Faculty Network Awards
  - Awards that promote new and to strengthen existing faculty networks that address global health disparities, such as efforts to strengthen partnerships with institutions in low- and middle-income countries, collect primary data, and develop strategies and policies for improving health and health care in resource-poor settings.

- https://medicine.yale.edu/yigh/faculty/grants/

- Yale Center for Outcomes Research and Evaluation (CORE)
  - National outcomes research center working on select projects designed to assess healthcare quality and evaluate clinical decision making and comparative effectiveness of specific healthcare interventions.
  - https://medicine.yale.edu/core/

- Yale Center for Tobacco Regulatory Science (TCORS)
  - Conducts research to inform tobacco regulation and includes experts in sensory perception, tobacco addiction, adolescent tobacco use, menthol and irritant receptor biology, nicotinic receptor biology, dopaminergic signaling in brain reward pathways, human behavioral pharmacology, assay and clinical pharmacokinetics, analytical chemistry, health economics and decision-making science and includes faculty from the schools of medicine, public health, and arts and sciences
  - https://medicine.yale.edu/psychiatry/tobacco/tcors/

- Yale Pepper Older Americans Independence Center
  - An inter-departmental, multidisciplinary center that promotes functional independence of older Americans by increasing scientific knowledge related to multifactorial geriatric conditions, advancing the science of clinical decision making in multimorbid adults, and educating and training new investigators in research on aging from a multifactorial perspective.
  - https://medicine.yale.edu/intmed/geriatrics/peppercenter/

- The Translational Targeted Areas of Research Excellence (T-TARE)
  - Focused on providing administrative support and seed money to interdisciplinary teams in support of translational studies to generate preliminary data and evidence of collaboration sufficient to obtain extramural funding, such as multi-investigator R01, P01, or SPORE (P50) grants.
  - https://www.yalecancercenter.org/research/excellence/ttare/

- Women's Health Research at Yale
  - The university's interdisciplinary research center advancing the health of women and our knowledge of the interplay of sex, gender, and health. Since its inception in 1998, the center has become a national model for launching research on the influence of sex and gender on human health, translating findings into practice, sharing health information with the public and policymakers, and providing mentored training in interdisciplinary team science.
  - http://medicine.yale.edu/whr

EXEMPLARS AT OTHER INSTITUTIONS

- Koch Institute for Integrative Cancer Research at MIT
  - Brings together biologists and chemists along with biological, chemical, mechanical, and materials science engineers, computer scientists, clinicians, to bring fresh perspectives and

an interdisciplinary approach to advancing the fight against cancer.
    - https://ki.mit.edu/

- Stanford Bio-X
    - Program supporting research and educational opportunities that cross disciplines between the biological or biomedical sciences and fields of engineering, physics and computational science.
    - https://biox.stanford.edu/

EXEMPLAR TRAINING GRANTS AT YALE

- National Clinicians Scholars Program (previously Robert Wood Johnson Scholars Program)
    - A 2-year interprofessional fellowship for physicians and doctorate prepared nurses designed to prepare future clinician leaders. Scholars gain research and leadership skills to change health policy and health care.
    - https://medicine.yale.edu/intmed/nationalcsp/

- The Yale and Yale-New Haven Hospital Center for Outcomes Research and Evaluation (Yale-CORE)
    - Patient-Centered Outcomes Research (PCOR) Scholars Program
    - a comprehensive, interdisciplinary, individualized, mentored career development program that positions individuals to create transformational health care improvement through their research and its application.
    - https://medicine.yale.edu/core/education/k12/

- Yale Center for Clinical Investigation Multidisciplinary Pre-and Post-Doctoral Training Program
    - Trains pre- and post-doctoral trainees from medicine, nursing, public health, and biomedical engineering in clinical and translational research.
    - https://medicine.yale.edu/ycci/education/predoc/
    - https://medicine.yale.edu/ycci/education/internshipaddprograms/postdoc/

- Yale School of Public Health Post-Doctoral Training in Cancer Prevention and Control
    - This multidisciplinary fellowship will train post-doctoral fellows in cancer etiology, cancer outcomes, lifestyle behavioral interventions, implementation science, and community-engaged research.

- Yale Center for Implementation Science
    - This multidisciplinary fellowship trains junior faculty and post-doctoral fellows in dissemination and implementation
    - https://medicine.yale.edu/ycis/scholars/about/

- Geriatric Clinical Epidemiology and Aging Related Research (T32)
    - The training program provides highly qualified fellows (MDs or PhDs) with opportunities to expand their skills in clinical epidemiology and aging research and to embark upon an intensive research experience under the mentorship of experienced investigators in gerontology and geriatric medicine.

- Research Training in Childhood Neuropsychiatric Disorders (T32)

- This program seeks to support the development of the next generation of translational researchers, from both basic and clinical sciences who are committed to discovering disease- related genes, key environmental factors, biomarkers, and to developing novel treatments and preventive interventions in developmental neuroscience. A major focus of the training is to promote dialogue across disciplines and emphasize the importance of interdisciplinary teams.