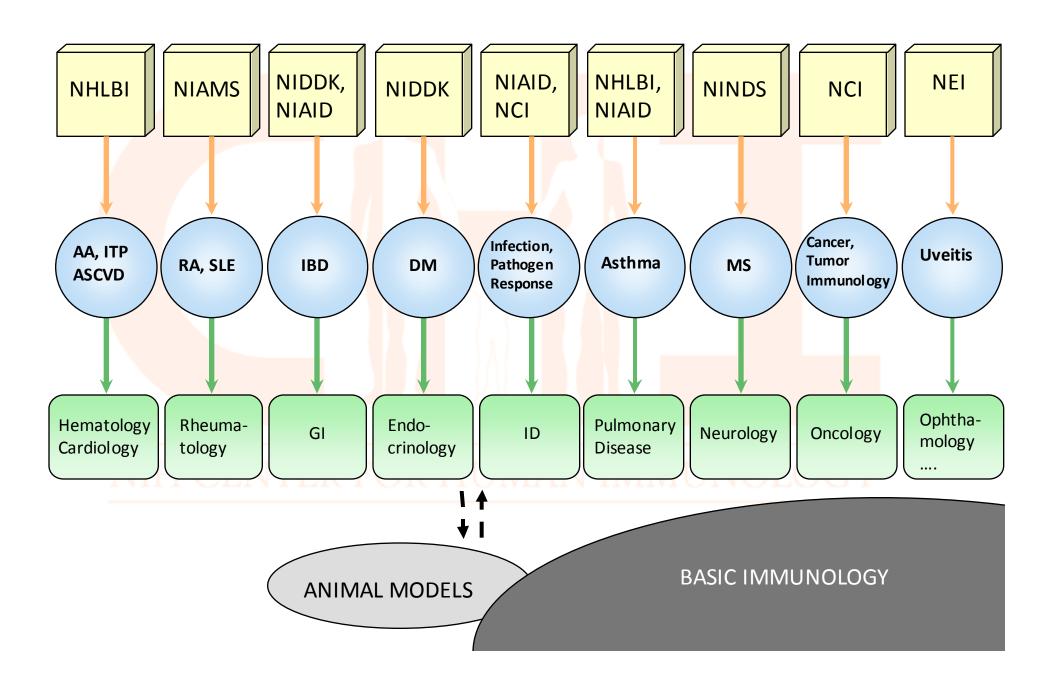
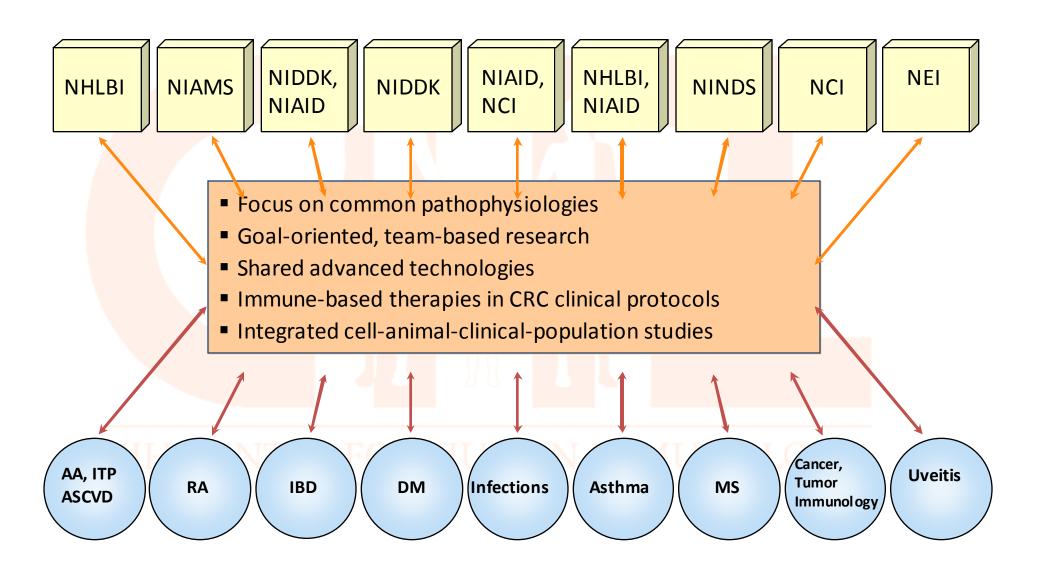
# TRANS-NIH CENTER FOR HUMAN IMMUNOLOGY, AUTOIMMUNITY, AND INFLAMMATION (CHI)



#### **CURRENT FRACTURED APPROACH TO CLINICAL IMMUNOLOGY RESEARCH**



#### A NEW PARADIGM FOR PATHOPHYSIOLOGY-ORIENTED RESEARCH



## MAJOR AND DISTINCTIVE FEATURES OF CHI

• Human biology as field of study/clinically motivated

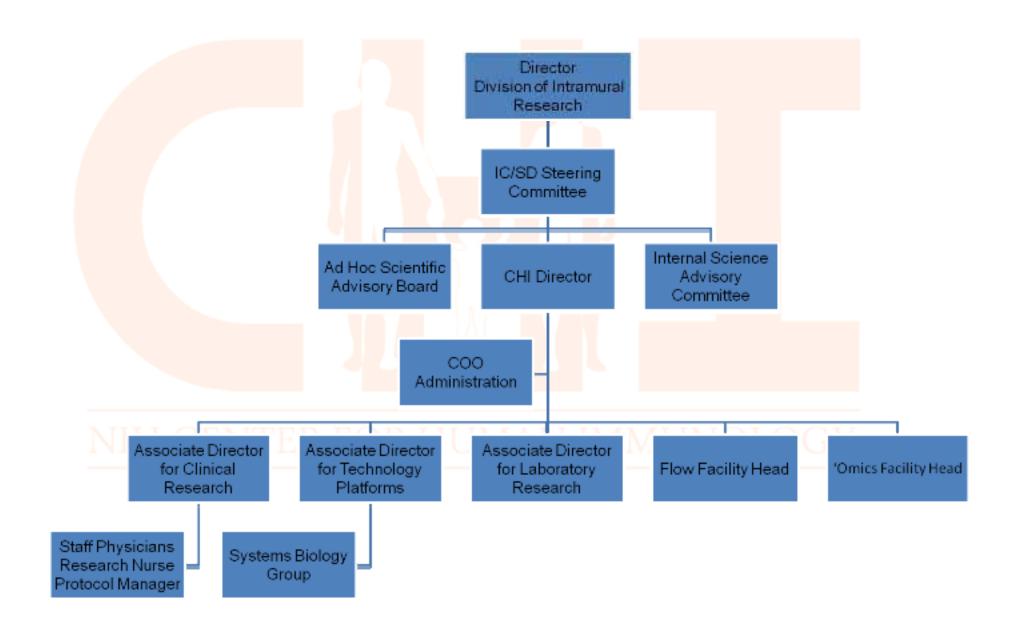
Goal-oriented, team approach for basic scientists/clinicians

• Incorporation of new technologies/expert technical staff/infrastructure

#### **CHI: ADDITIONAL BENEFITS**

- Develop unique training program in clinical immunology
- Create a culture of coordination:
- within NIH
- NIH-extramural academia
- NIH-Biotech/Pharma
- Recruit next generation NIH physician-scientists/clinical investigators
- Increase *clinical activity* in CRC
- New efficiencies for clinical research from utilization of advances in large scale data generation/quantitative analysis

# **CHI ORGANIZATION**



## **CHI PERSONNEL**

Neal Young, M.D., Head Giorgio Trinchieri, M.D., Associate Director for Laboratory Research Dan Kastner, M.D., Associate Director for Clinical Studies Ron Germain, Associate Director for Technology Platforms

\*Howard Dickler, M.D., Chief Operating Officer

\*Christen Norris, B.A., Administrative Assistant

J Philip McCoy, Ph.D, Chief, Flow Platform Facility

\*Angelique Biancotto, Ph.D., Staff Scientist

\*J Chris Fuchs, BS, Biologist

Francesco Marincola, M.D., Chief, -Omics Facility Ena Wang, M.D., co-Director \*Faribia Chinian, M.S., Biologist

\*Matthew Olnes, M.D.. Staff Physician

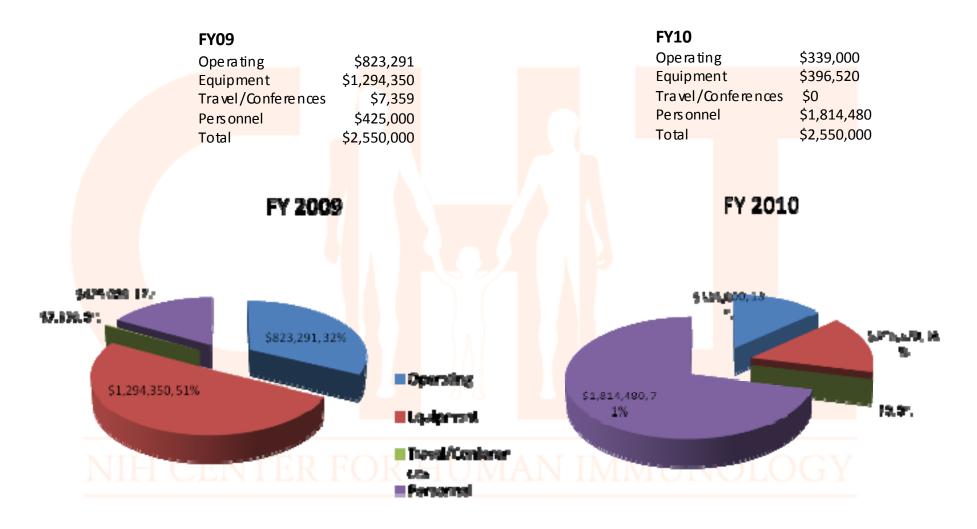
\*Shira Perl, M.D., Staff Physician

#### Vacant:

Research nurse
Protocol manager
Systems biologists (3-4)

\*full-time CHI employee

# CHI BUDGET, FY09-FY10



Notes: 1) FY10 "Equipment" available for operating and other expenses; 2) Travel/Conference funds uncommitted

# CHI SPACE, CURRENT AND PLANNED



65% drawing completion estimated November 2010

# **PLATFORM FACILITIES**

#### Flow Cytometry

clinical assays adapted for immune system cells intracellular cytokines and phosphoproteins for function circulating cytokines tetramer staining flow-based imaging

#### -Omics

high throughput sequencing-based analysis of transcriptome high density SNP arrays for genetic associations epigenomic analysis using ChIP-Seq high throughput sequencing ("\$1000 genome") proteomics (shared with PSIIM)

#### **Clinical Protocol**

"deep" phenotyping of healthy humans ("immunome") and patients intensive assessment of limited numbers of subjects observation and intervention studies; new protocols and supplements to existing studies

**Computational/Systems Biology** 

# CHI FLOW CYTOMETRY PLATFORM

#### Personnnel:

J Philip McCoy, Ph.D., Director Angelique Biancotto, Ph.D., Staff Scientist J Chris Fuchs, B.S., Biologist



#### **Instrumentation:**

5 laser, 18 color LSRII Fortessa cytometer w/HTS 3 laser, 13 color FACSAria II cell sorter Luminex 100 cytometer

## **'OMICS PLATFORM FACILITY**

#### Personnel

Francesco Marincola, M.D., Director Ena Wang, M.D., Staff Scientist \*Fariba Chinian, M.S., Biologist

### **Equipment**

Solexa Genome Analyzer XII (Solexa sequencer)
Illumina iScan (Beadstation)
Affymetrix Genechip Scanner 7G
Agilent Array Scanner
GeneMachine Omnigrid array printer
LabChip GXII and Agilent Bioanalyzer

<sup>\*</sup>CHI employee

## **SYSTEMS BIOLOGY EFFORTS**

CHI is budgeted for 3-4 computational biologists: our major laboratory effort

Group would include: informatics, database, modeling expertise

Recruiting efforts: second advert (including on-line services); government notice of positions available; Tsang tasked

## **H1N1 VACCINE PROTOCOLS**

NIH employees, >18 years old, through Occupational Medical Services

N = 200; volunteers paid and vaccination pre-scheduled

Clinical and routine laboratory phenotyping

Pre-vaccine samples (x2) will provide an early healthy control database

Post-vaccine at days 1, 7, 14, 28, 60

Frozen cells, plasma, sera, nasal washes

Flow panel for B, CD4, CD8, NK, Tregs; plasma cytokines; IC cytokines (TH1, TH2, TH17, Treg)

Viral antigen response: antibodies, B cell ELISPOT, T cell peptide response, tetramer binding (?)

-Omics for immune response gene polymorphisms, transcriptome arrays of T cell subsets

Associated subset studies: intensive early analysis of innate immune response confirmed flu cases among volunteers and CC patients

Hypothesis: Can we detect meaningful changes in immune response?

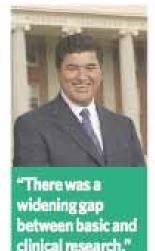
CHI pilot: Logistics, coordination, extramural-pharma interactions

# **PLANS**

- 1. Immunome in healthy humans
- 2. Other vaccine trials: repeat yellow fever, other arboviruses; experimental vaccines
- 3. Protocols for drug interventions and the immune response
- 4. Additional data for shared mechanisms/pathophysiologies/biomarkers among autoimmune and inflammatory diseases including cancer
- 5. Family autoimmune disease clinic
- 6. Interventional trials: type 1 diabetes, novel agents from industry
- 7. Collaboration with extramural investigators to utilize Clinical Center
- 8. Training program in clinical immunology

#### NIH'S COMMITMENT TO "TRANSLATIONAL" RESEARCH AND CHI





Elias Zerhouni

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Under the direction of Elias Zerhouni, the US National Institutes of

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Health is spending several hundred million dollars to set up translational research centres across the United States (see page 840). At this early stage, it's not clear whether this represents a game-changing commitment by the agency and the receiving institutions, or an attempt to mollify tax-payers who want a return on their heavy investment. Many of the aims are the right ones, and anything is better than the current

situation in which an individual's publications trump real medical needs. But Zerhouni's successor in the next presidential administration must make it a priority to continue or surpass these efforts. Because translational research is a new and unproven discipline, with no 'how-to' manual, it is also important to evaluate each attempt at translation as the field takes shape.

A chasm has opened up between biomedical researchers and the patients who need the discoveries. Declan Butter asks how the ground shifted and whether the US National Institutes of Health can bridge the gap.

of Health, not the medical Research, or the National Institutes of Basic Biomedical Revearch." This tab, by molecular biologist Alan Schochter at the NEEL

**NEWS FEATURE** TRANSLATIONAL RESEARCH

is a pointed one. The organization was formally established in the United States more than half a century ago to serve the nation's public health, and its relation now is to rursus fundamental knowledge and apply it "to reduce the burdens of fines and disability". So when employees at the agency have to check their name tag, some soul searching must be taking place.

There is no question that the NIH excels Schoolter are asking is whether it has neglected the mandate to apply that knowledge. Outside the agency too there is a growing perception that the enormous revocators being put into biomedical research, and the buge strides made in understanding disease mechanisms, are not resulting in commensurate poins in new treatments, diagnostics and prevention.

"We are not seeing the breakthrough therapies that people can rightly expect," says Schediter, head of molecular biology and genetics at the National Institute of Diabetes and Diagnitive and Kidney Diseases in Bethesda, Maryland.

Medical-research agencies worldwide are experiencing a similar avakening. Over the part 30 or so years, the ecosystems of basic and clinical research have diverged. The pharin basic research. What researchers such as - majoratical industry, which for many years was expected to carry discoveries across the divide, is now hard pushed to do so. The abyes

left behind is sometimes labelled the 'valley of death' - and neither basic researchers. busy with discoveries, nor physicians, busy with putients, are keen to venture there. "The clinical and basic scientists don't really communicate," sun Barbara Abring, director of the NIH's National Center for Research Resources in Bethewla.

Alving is a key part in the NIIT's attempt to bridge the gap with 'translational research'. Director Elias Zerbouni made this bridgebuilding a focus in his signature 'roadmap' for thragency, announced in 2005 (see Nature 425, 438 2005). Spearheading the NIH offert will be a consortium of 60 Clinical and Translational Science Centers (CTSCs) at universities and medical centres across the country, which will share some USBNO million annually when they are all in operation by 2012. Late last mouth, the NIH doled out the most recent grants in

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NIH CENTER FOR HUMAN IMM

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Big science! Immunology?