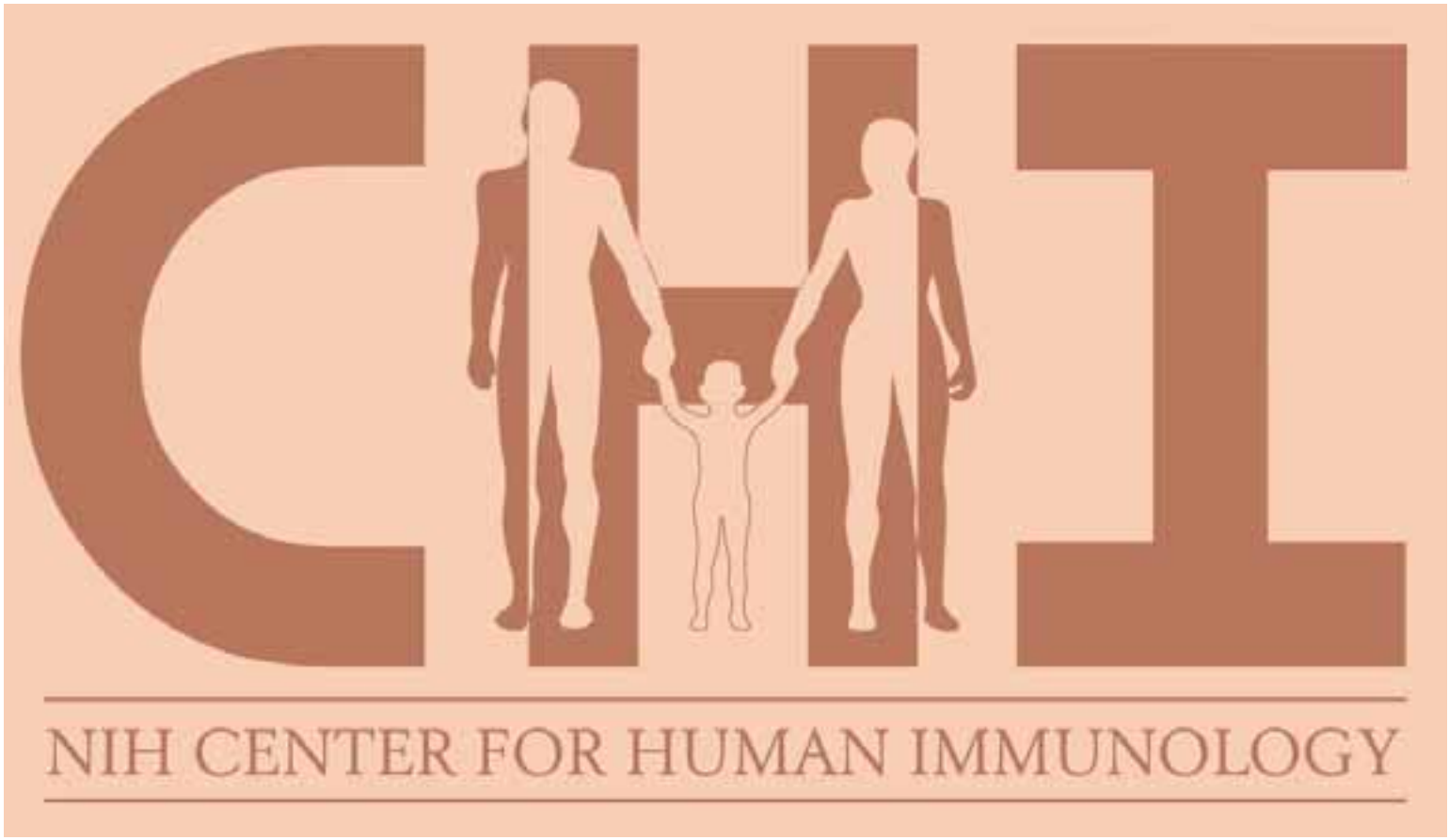
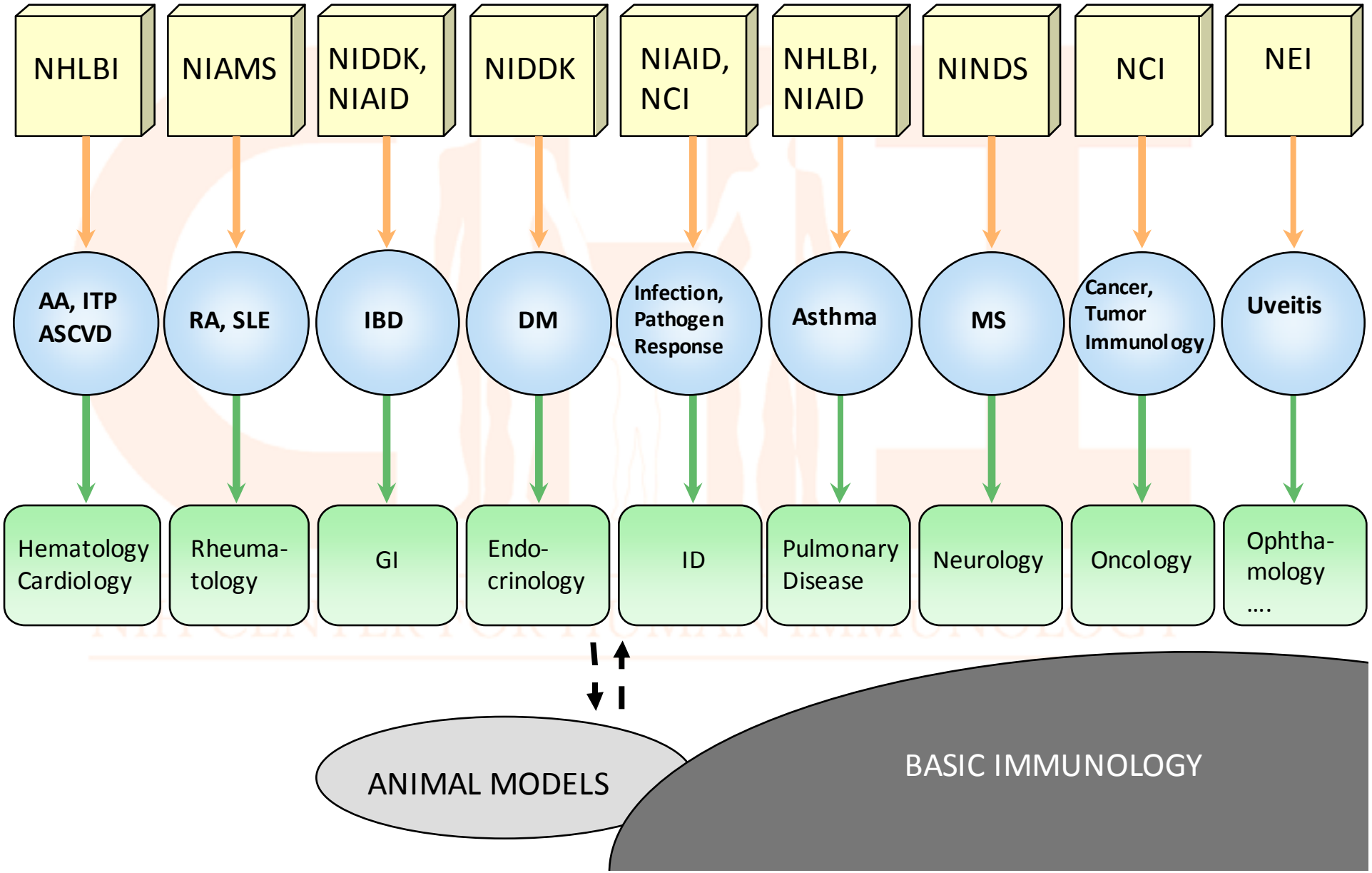
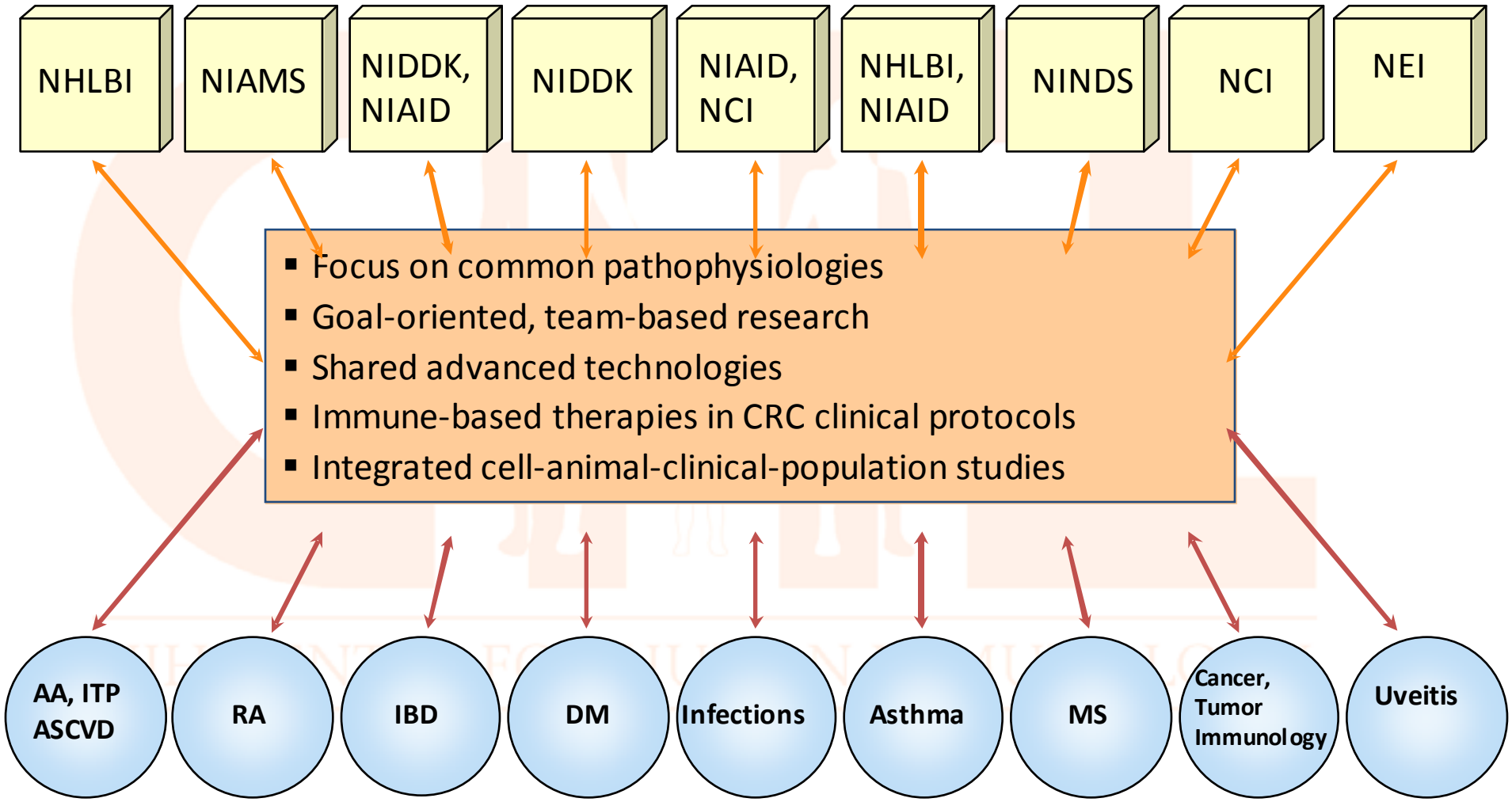
TRANS-NIH CENTER FOR HUMAN IMMUNOLOGY, AUTOIMMUNITY, AND INFLAMMATION (CHI)



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

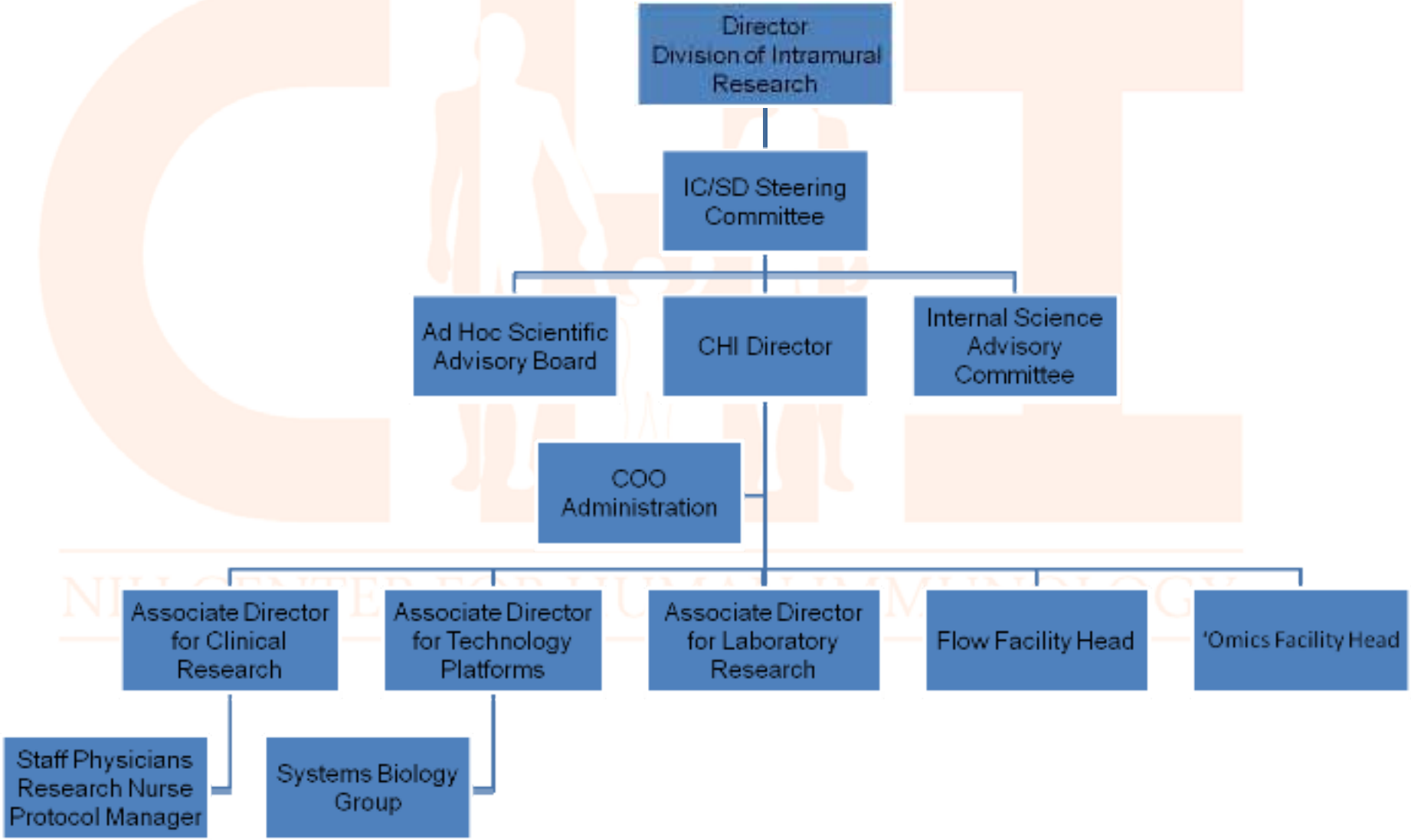
- Create a *culture of coordination*:
- within NIH
- NIH-extramural academia
- NIH-Biotech/Pharma

- *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***

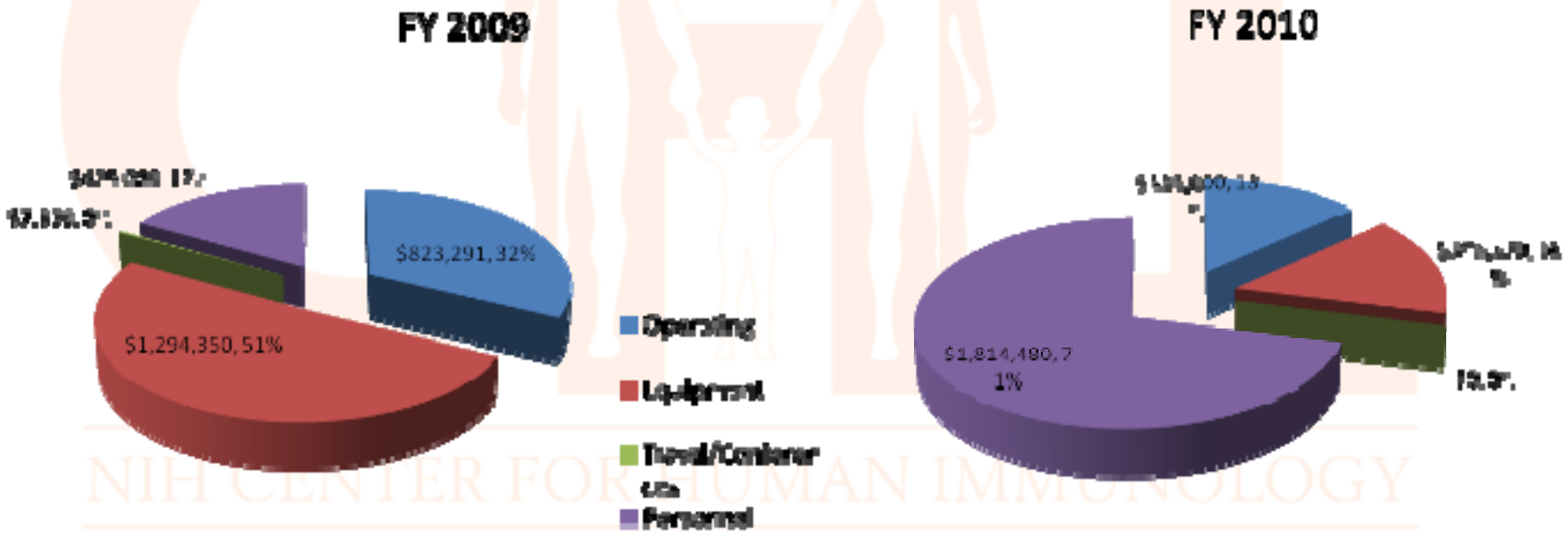
CHI BUDGET, FY09-FY10

FY09

Operating	$823,291
Equipment	$1,294,350
Travel/Conferences	$7,359
Personnel	$425,000
Total	$2,550,000

FY10

Operating	$339,000
Equipment	$396,520
Travel/Conferences	$0
Personnel	$1,814,480
Total	$2,550,000



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

<u>Personnnel:</u>
J Philip McCoy, Ph.D., Director
Angelique Biancotto, Ph.D., Staff Scientist
J Chris Fuchs, B.S., Biologist

<u>Instrumentation:</u>
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

****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

12 June 2008

agency

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

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NEWS>>

Neandertal population genetics 252

NOMINATIONS

White House Taps Former Genome Chief Francis Collins as NIH Director

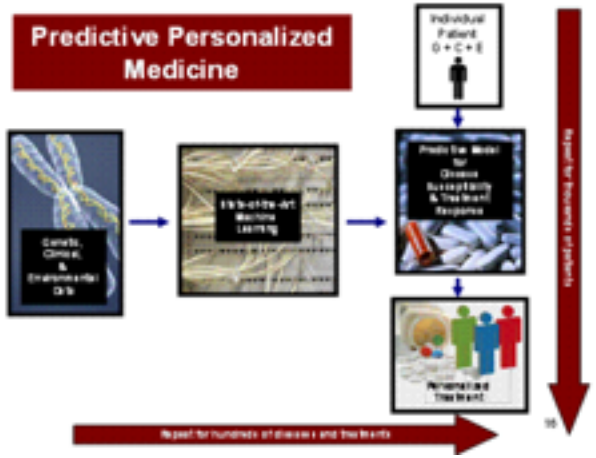
President Barack Obama's announcement last week that he had chosen Francis Collins to lead the National Institutes of Health (NIH) did not come as a big surprise. But it ended months of speculation and ignited a volley of fluttering remarks from researchers and biomedical groups. "Francis is one of the most accomplished scientists and scientific leaders of his generation. ... Having worked with him for many years, I am sure that he will rise to the unique challenges of this job," said Elias Zerhouni, who resigned as NIH director last fall.

Collins is known as a skilled administrator and excellent communicator. Over 15 years, he built a new center at NIH into one of the most visible and innovative institutes. When he stepped down as leader of the National Human Genome Research Institute (NHGRI) last year, he was already considered a leading candidate to run NIH, the $30 billion parent agency.

Although few would disagree with a White House press release saying that Collins's work "has changed the very ways we consider our health and examine disease," Collins does have critics. Some question his support of "big biology" in the genome project portfo-

QUESTIONS ABOUT THE LANGUAGE OF GOD

Although many scientists say president Francis Collins will make a superb director of the National Institutes of Health (NIH), not everyone is celebrating. A discussion about whether Collins's very public religious views will influence his leadership of NIH played out on blogs



Big science! Immunology?