

Clinical Research at the CC: Past and Present



“There is no other hospital like it”

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**Chief Scientific Officer Clinical Center
NIH Associate Director for Clinical Research**



What makes us different?

- **Our Vision**

President Harry Truman Lays Corner Stone

June 22, 1951



“Modern medicine must find ways of detecting diseases in their early stages and of stopping their destructive force. That will be the major work in this clinical research center.”

What makes us different?

- **Our Vision**
- **Free care**
- **Every patient participates in one of our ~1500 clinical research protocols**

What makes us different?

- Our Vision
- Free care and Every patient participates in one of our 1500 clinical research protocols
- **A hospital surrounded by research laboratories**
 - 33 Lasker awards
 - 7 Nobel laureates

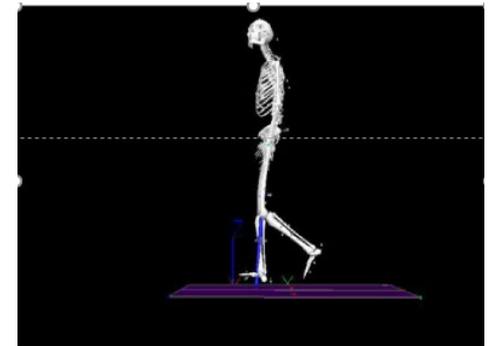
1953-Medical Board



Issued: “Guiding Principles in Medical Research Involving Humans” required prospective review of all human research at the Clinical Center including a detailed review of the informed consent process. The policy later served as the basis for National IRBs.

What makes us different?

- Our Vision
- A hospital surrounded by research laboratories
- **Special resources to enable studies**
 - Biomechanics laboratory
 - Metabolic chambers
 - Center for Cellular Engineering
 - MRI center-30 MRI in or adjacent to CC
 - PET research-3 cyclotrons
 - High containment clinical studies unit
 - Strong healthy volunteer program
 - Bioethics department



***SELECTED* ACCOMPLISHMENTS**

Cancer

1958

- Cure of choriocarcinoma with methotrexate, first treatment of a human solid tumor.

*Min Chiu
Li*



*Roy
Hertz*



1964

- Cure of childhood acute lymphocytic leukemia.

*Emil
Frei*



*Emil
Freireich*



1965

- Chemotherapy for Cancer

*Vincent
DeVita*



*James
Holland*



*John
Ziegler*



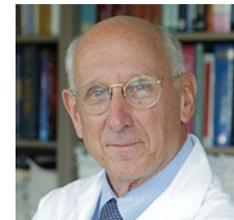
*Gordon
Zubrod*



1988

- Metastatic melanoma first treated with cell transfer therapy and later shown to give a durable and complete response.

*Steven
Rosenberg*



Cancer continued

1993

- Genetic basis and management of hereditary kidney cancer.

Marston Linehan



2001

- Immunotoxin BL22 to treat Hairy Cell Leukemia

Ira Pastan



Robert Kreitman



2008

- MRI-ultrasound fusion guided prostate biopsy

Peter Pinto



Bradford Wood



Peter Choyke



2017

- (CAR) T-cells to treat lymphoma

James Kochenderfer and colleagues



Transfusion Medicine

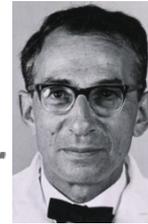
1956

- Coulter Model S automatic blood counter.

Wallace Coulter



George Brecher



1961

- 1st Plasmapheresis and source of platelets.

Allan Kliman



1965

- Continuous flow blood separator.
George Judson (IBM)
with *Emil Freireich*



1964

- Australia antigen discovered.

1970

- Blood bank switches to all-volunteer donors.
- reduces post transfusion hepatitis from about 30% to 11%.

1989

- Hepatitis C virus discovered.

Harvey Alter



Hematology and Sickle Cell Anemia

1995

- Treatment of aplastic anemia with anti-thymocyte globulin and cyclosporine.

*Neil
Young*



- Hydroxyurea for sickle cell anemia.

*Griffin
Rodgers*



2019-2022

- Bone marrow transplant and gene therapy for sickle cell anemia.

*Courtney
Fitzhugh*



*John
Tisdale*



Heart Disease

1957

- Idiopathic hypertrophic subaortic stenosis discovered.

Gene Braunwald



Glen Morrow



1960

- First successful mitral valve replacement.

Nina Starr Braunwald

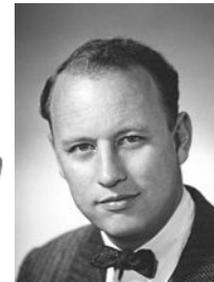


Glen Morrow

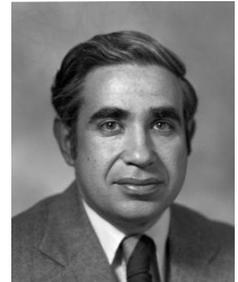
1961

- The genetic basis of Tangier Disease, classification of lipid diseases, high lipids as risk factor for coronary heart disease.

Donald Fredrickson



Robert Levy



2022

- Leptin-replacement for lipodystrophy

Philip Gordon



Infectious Diseases- 7 Vaccines

1987

- *H. influenzae* meningitis vaccine.

Rachel Schneerson



John Robbins



1972-1994

- Hepatitis A, Hepatitis B, Rotavirus vaccines.

Stephen Feinstein, Albert Kapikian, Robert Purcell



2005

- HPV vaccine technology.

John Schiller



Douglas Lowy



1997

- Ebola vaccine/1st in human.

Gary Nabel



Barney Graham



2020

- COVID-19 technology/1st in human.

Kizzmekia Corbett, Barney Graham



Infectious Diseases-AIDS

1982–1985

- Immunopathogenesis of HIV.

*Anthony
Fauci*



*Cliff Lane
and
colleagues*



- Screening test for HIV (HTLV-III).

*Robert
Gallo*



First Treatments for HIV

- 1987 - AZT as first treatment.
- 1988 - 2',3' dideoxycytidine or ddc.
- 1990 - 2',3' dideoxyinosine or ddi.



*Sam
Broder*

1984–2022

- Genetic sequence and new diagnostic tests for *P. carinii* pneumonia.

*Joseph
Kovacs*



- National Guidelines for Management of HIV

*Henry
Masur*



Infectious Diseases plus Ebola and COVID-19

1982

- **Clinical trial of acyclovir to treat genital and oral herpes.**

*Stephen
Straus*



2021

- **Survival of COVID patients in 558 US hospitals Interhospital transfer of COVID patients safe.**

*Sameer
Kadri*



2022

- **Persistent SARS-COV-2 in human brain as long 230 days post symptoms (autopsy study). (*Nature*, In Press)**

*Daniel
Chertow*



Infectious Diseases/Immunology cont.

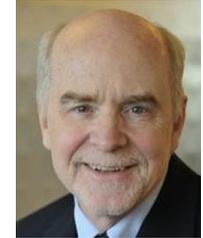
2021

- JAK inhibitors to treat autoimmune, allergic, and COVID-19.

*Warren
Leonard*



*John
O'Shea*



1994

- Sustained release ganciclovir implant for cytomegalovirus retinitis.

*Robert
Nussenblatt and
colleagues*



1997

- Microbial genomics to understand hospital infection outbreaks.

*Julie
Segre*



*Tara
Palmore*



*David
Henderson*



Mental Illness

1969

- Clinical trials of lithium for depression and mania.

*Frederick
Goodwin*



1977

- 2-deoxy-D-glucose and development of PET scanning.

*Louis
Sokoloff*



1985

- Description and 1st treatment of obsessive-compulsive disorder (clomipramine).

*Judy
Rapoport*



1994

- 1st treatment of childhood schizophrenia (clozapine)

1998

- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS).

*Susan
Swedo*



Mental Illness cont.

2010

- Ketamine for depression and suicidal ideation.

*Carlos
Zarate*



2016

- Esketamine for depression (without addiction).

2012

- Premenstrual Dysmorphic Disorder and treatment with fluoxetine.

*Peter
Schmidt*



*David
Rubinow*



2020

- Disruptive Mood Dysregulation Disorder described in children to differentiate irritability from pediatric bipolar disorder.

*Ellen
Leibenluft*



2012–2021

- Suicide risk tool kit

*Maryland
Pao*



Endocrine

1972

- Insulin receptors discovered.

Jesse Roth



1985

- Cushing's syndrome treatment with glucocorticoid antagonist RU 486.

Lynnette Nieman



Lynn Loriaux



2017

- Niemann-Pick Disease treatment with intrathecal 2-hydroxypropyl-beta cyclodextrin.
- Importance of Melanocortin 3 receptor and neurotrophin factor in obesity.

Forbes D. Porter



Jack Yanovski



2013–2022

- Congenital adrenal hyperplasia management.

Debbie Merke



Techniques and Devices

1963

- Ommaya CNS reservoir.

*Ayub
Ommaya*



1969

- Method to locate parathyroid glands.

*John
Doppman*



2022

- Low cost 3D printed miniature ventilator.

*Andrew Mannes
and colleagues*



2016–2022

- External robotic devices to improve motor tasks in children with cerebral palsy.

*Diane
Damiano*



*Thomas
Bulea*



Summary

At the Clinical Center we have focused on three areas:

- **Pathophysiology of disease**
- **First in human with new drugs and devices**
- **Rare Diseases**

Future Challenges

- **Recruitment and retention of the best clinical researchers**
 - **Diversity, Equity, Inclusion and Accommodation**
 - **Observation: Not much diversity among investigators shown.**
 - 80 Investigators
 - 11 Women (14%)
 - 5 URM (6%), 3 African Americans (4%)
- **Budget**
- **Physical Plant**

Some Parting Questions for Discussion

- **Should we be able to study more infected patients during the next pandemic?**
- **Should there be more investment in social issues facing health such as health behavior and health disparities research?**

IMPACT OF RESEARCH AT THE CLINICAL CENTER

George Santangelo, PhD

Director, Office of Portfolio Analysis, NIH