



Of War, Mice, and Men

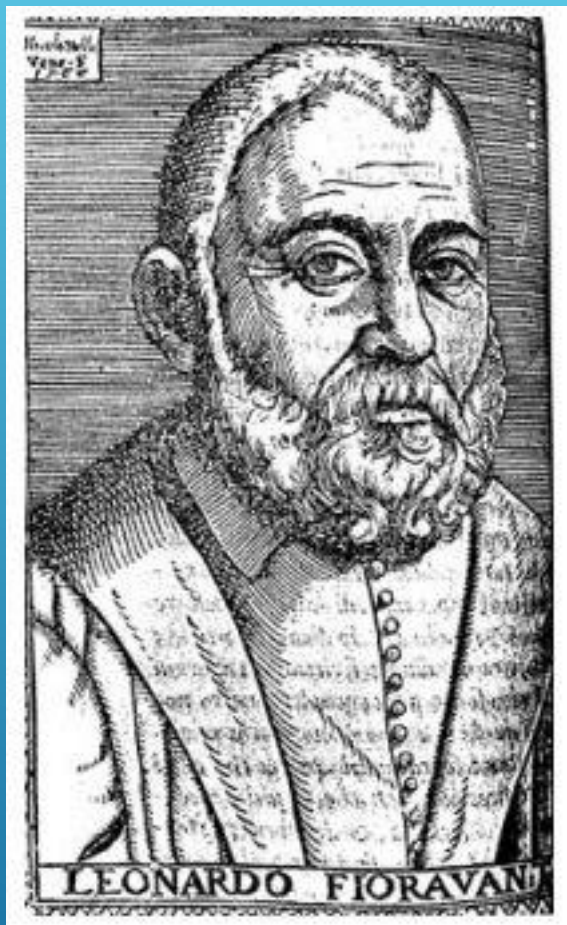
J. Harold Helderman, M.D.

यदा यदा हि धर्मस्य ग्लानिर्भवती भारत ।
अभ्युत्थानमर्धमस्य तदाऽऽत्मनं सृजाम्यहम् ॥



श्रीकृष्ण
२०१५





Renaissance Skin Grafting

Pietro and Paolo Viero from Calabria perfected skin transplants to the nose 16th century

Leonardo Fioravanti 1558 brought technique to Venice where it flourished

Important for response to frequent rhinotomy by sword




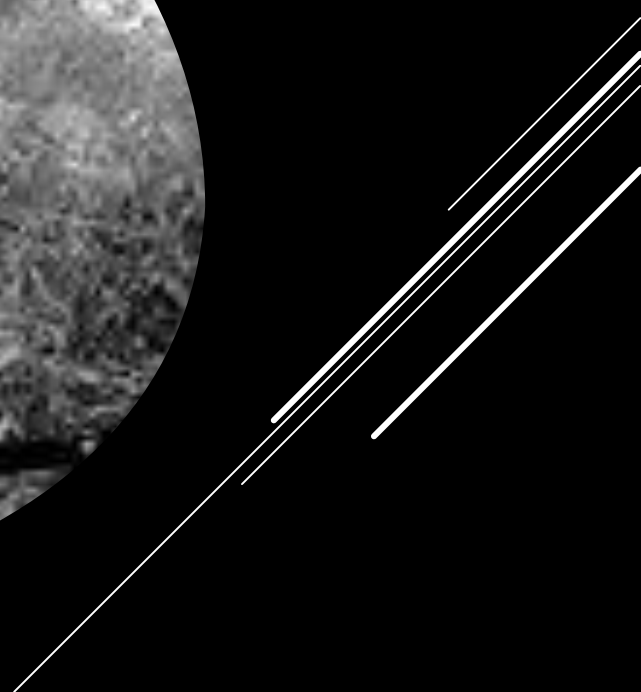




Franco-Prussian War

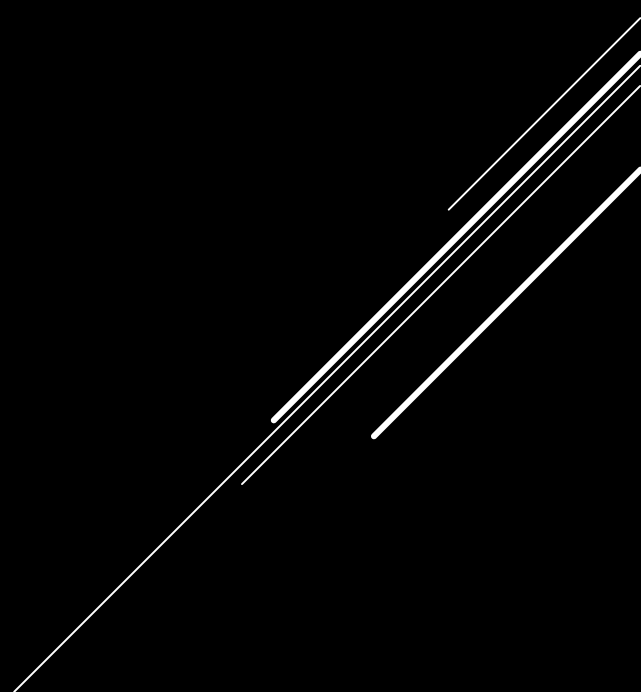
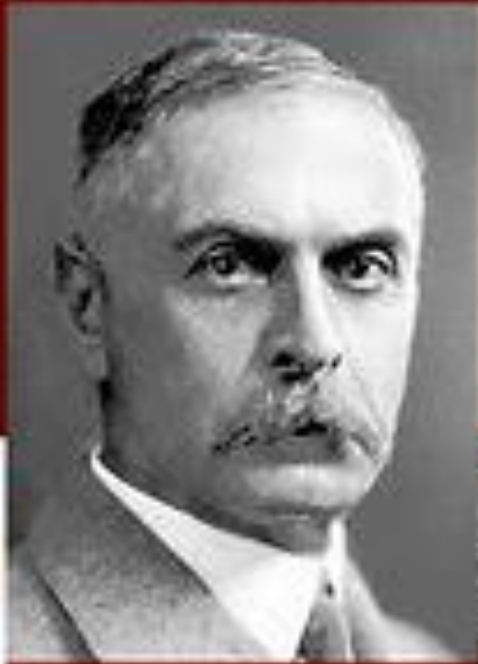
1870-1871

1. Bismarck and Wilhelm 1 defeat French and take Paris after Battle of Sedan
 2. Napoleon III captured and deposed
 3. Germany unified
 4. Battlefield surgical techniques of Pare employed
- 




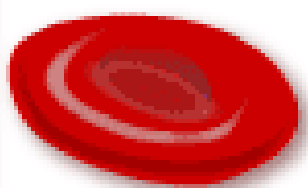
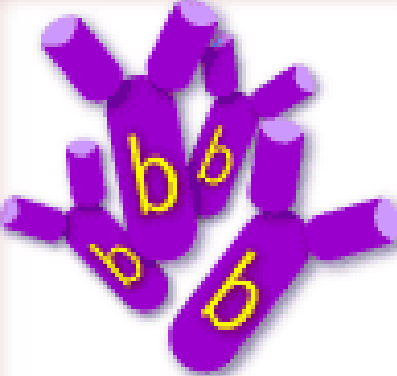

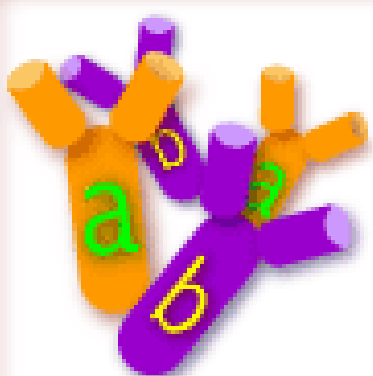




Karl Landsteiner (1868-1943)
The discoverer of Blood Groups



The ABO Blood System

Blood Type (genotype)	Type A (AA, AO)	Type B (BB, BO)	Type AB (AB)	Type O (OO)
Red Blood Cell Surface Proteins (phenotype)	 <p>A agglutinogens only</p>	 <p>B agglutinogens only</p>	 <p>A and B agglutinogens</p>	 <p>No agglutinogens</p>
Plasma Antibodies (phenotype)	 <p>b agglutinin only</p>	 <p>a agglutinin only</p>	<p>NONE.</p> <p>No agglutinin</p>	 <p>a and b agglutinin</p>

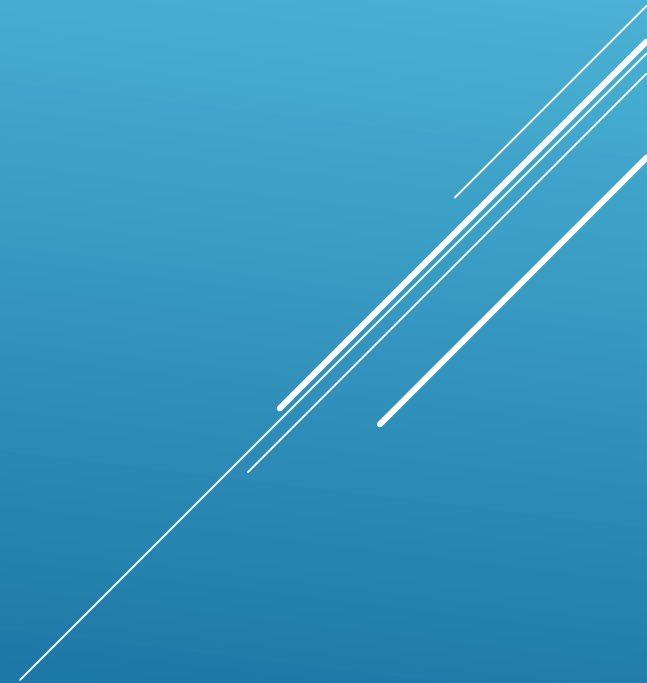


ALFR.
NOBEL

NAT.
MDCCC
XXXIII
OB.
MDCCC
XCVI

F. LINDBERG 1902









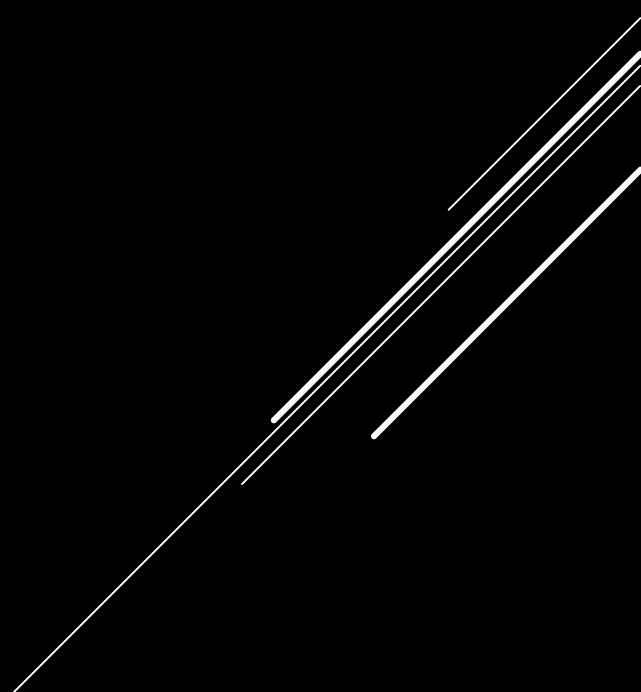


- The London Blitz ended on May 10, 1941. 32,000 civilians had died and 87,000 were seriously injured.





Lothar Baruch at the age of 10

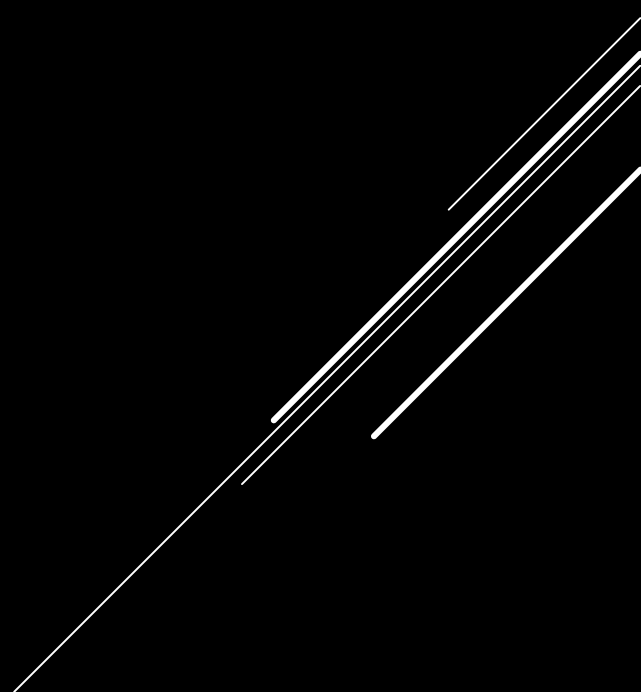




Leslie Brent at 21 years old

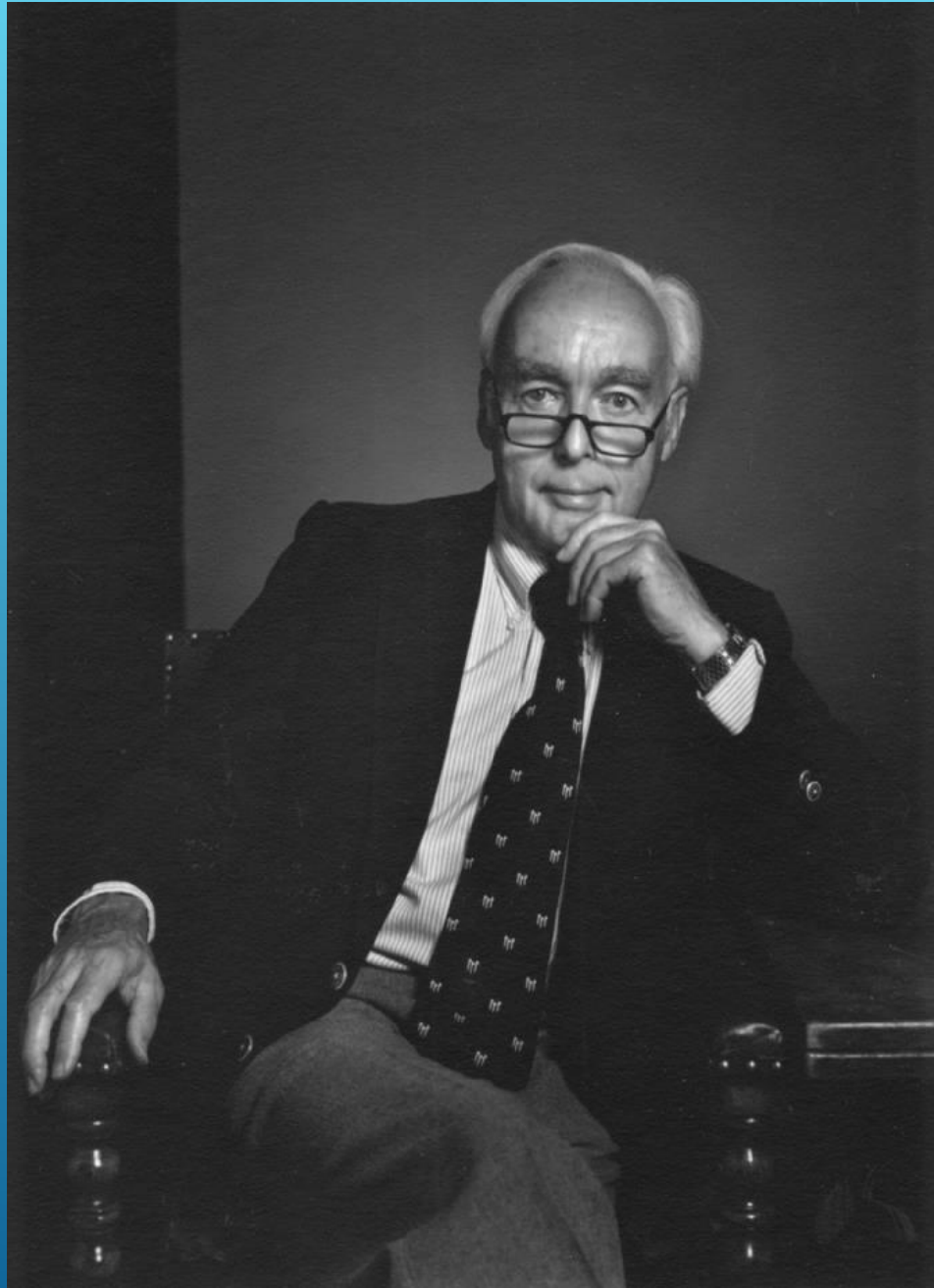


Sir Leslie Brent and Medawar





Leslie Baruch Brent in his 80th year The birth name, Baruch, was officially restored (as Brent's middle name) in the late 1990s





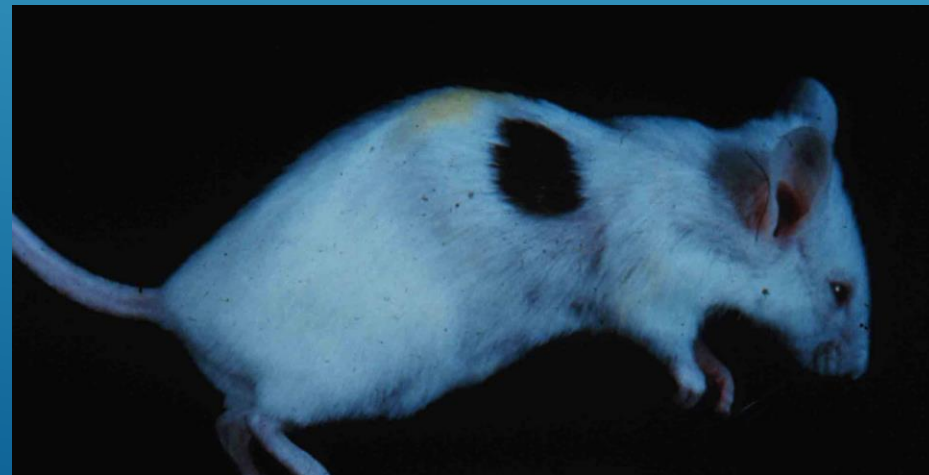
MEDAWAR'S CLASSIC ARTICLE

October 3, 1953 NATURE

‘Actively Acquired Tolerance’ of Foreign Cells

By Dr. R.E. Billingham*, L. Brent, and Prof. P.B. Medawar, F.R.S.

Department of Zoology, University College, University of London



TOLERANCE

**Specific Absence of an Immune Response
to Defined Stimulus (Antigen)**

Self Tolerance

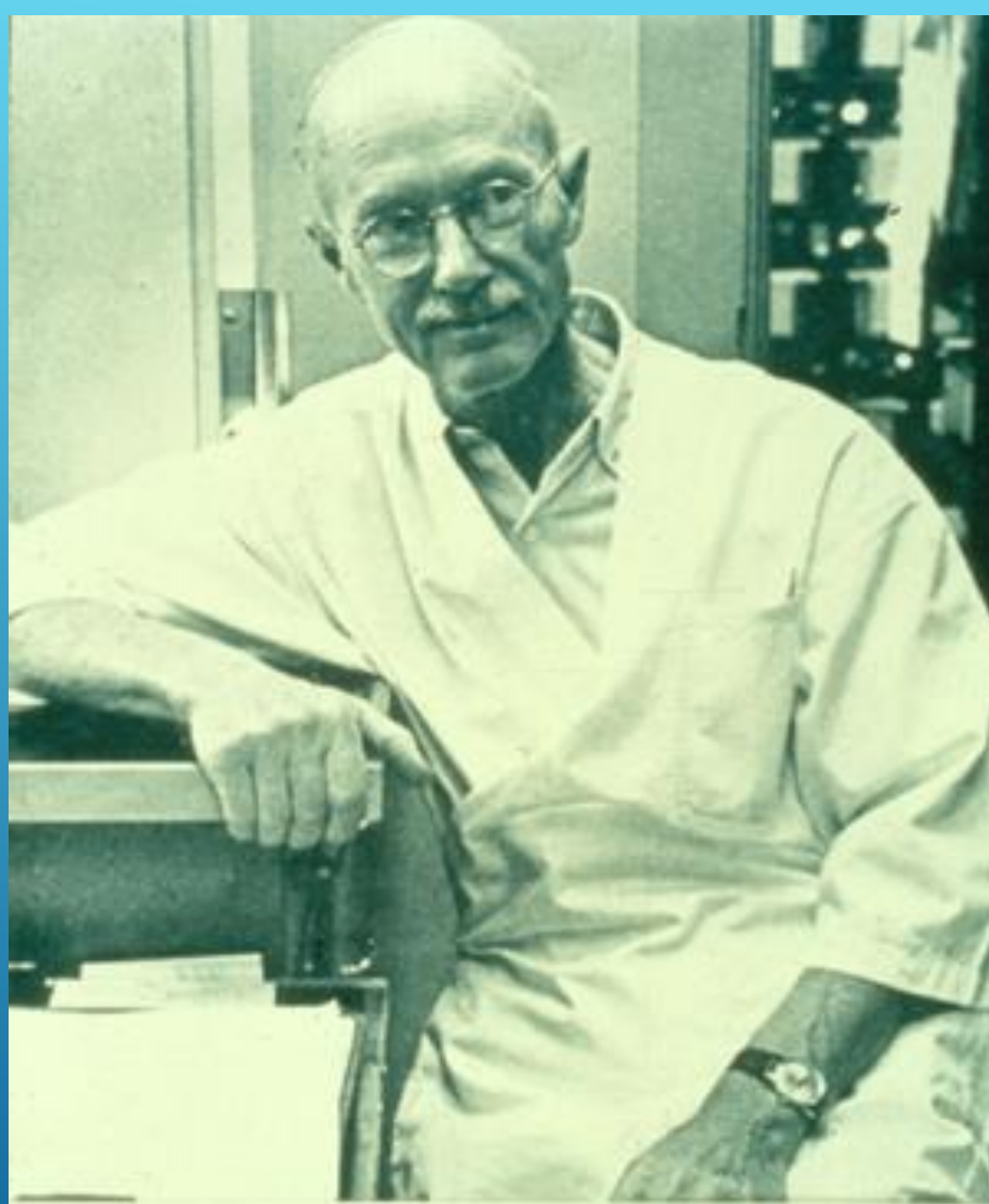
Tolerance to Foreign Antigen

- **Nominal Antigen**
- **Transplantation Antigen**

*Oh! To see Japan
naky ladies go crazy and dance on chairs.*

It has that





GEORGE D. SNELL 1903



MHC genes control graft rejection and immune responses

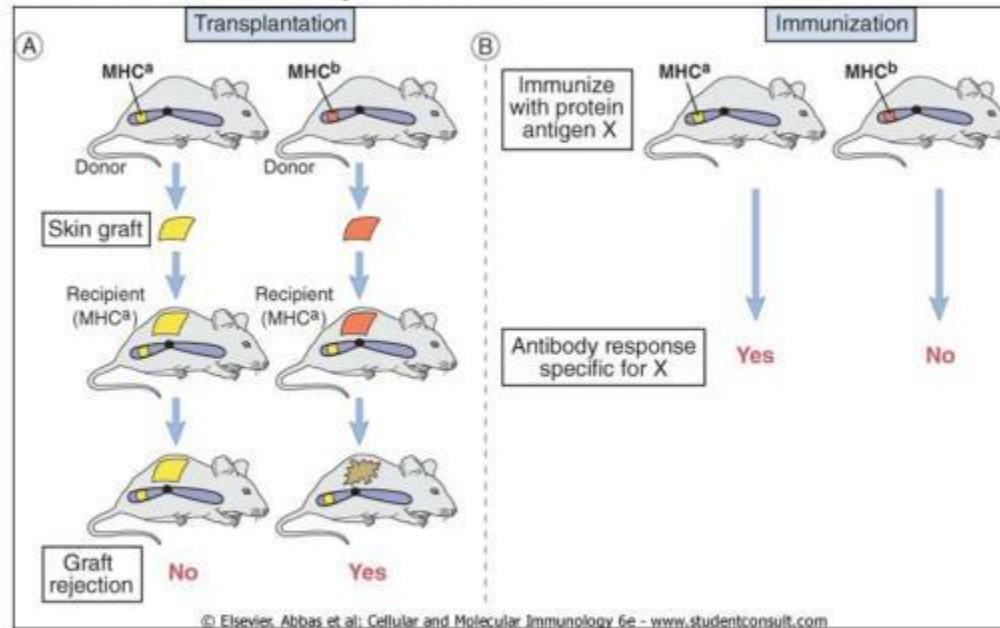
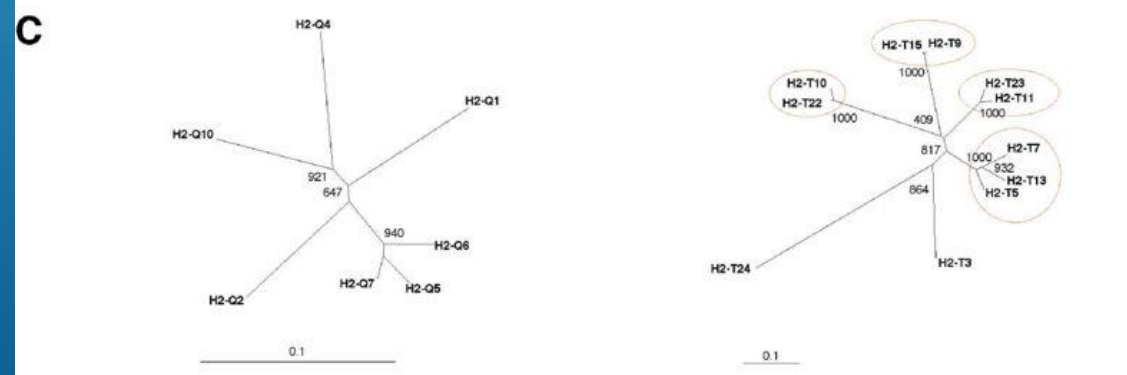
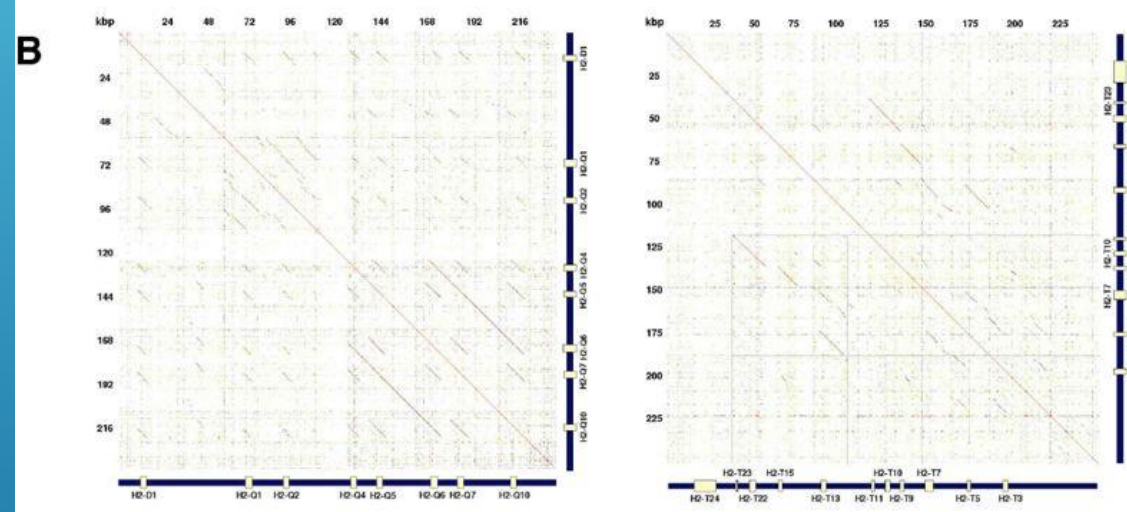
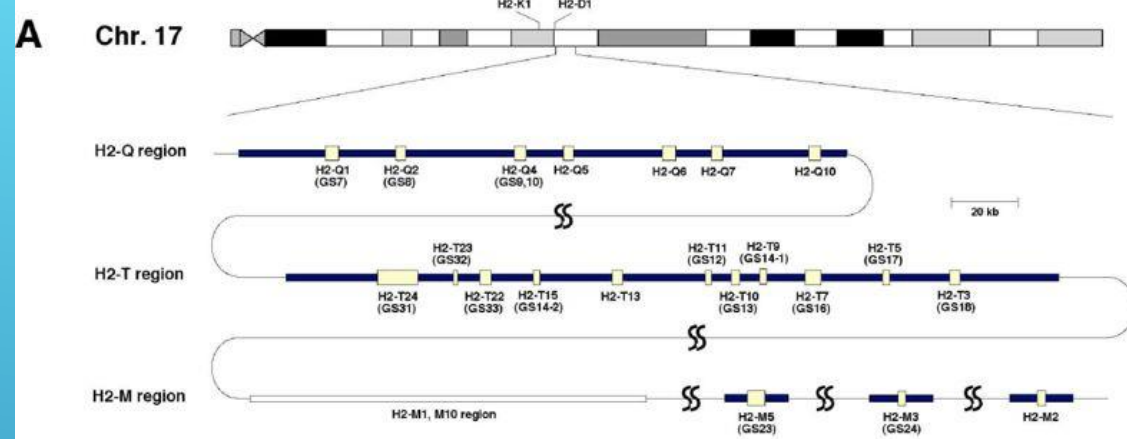


Figure 5-2 MHC genes control graft rejection and immune responses. The two strains of mice shown are identical except for their MHC alleles (referred to as a and b). These strains reject skin grafts from each other (A) and respond differently to immunization with a model protein antigen (usually a simple polypeptide) (B).



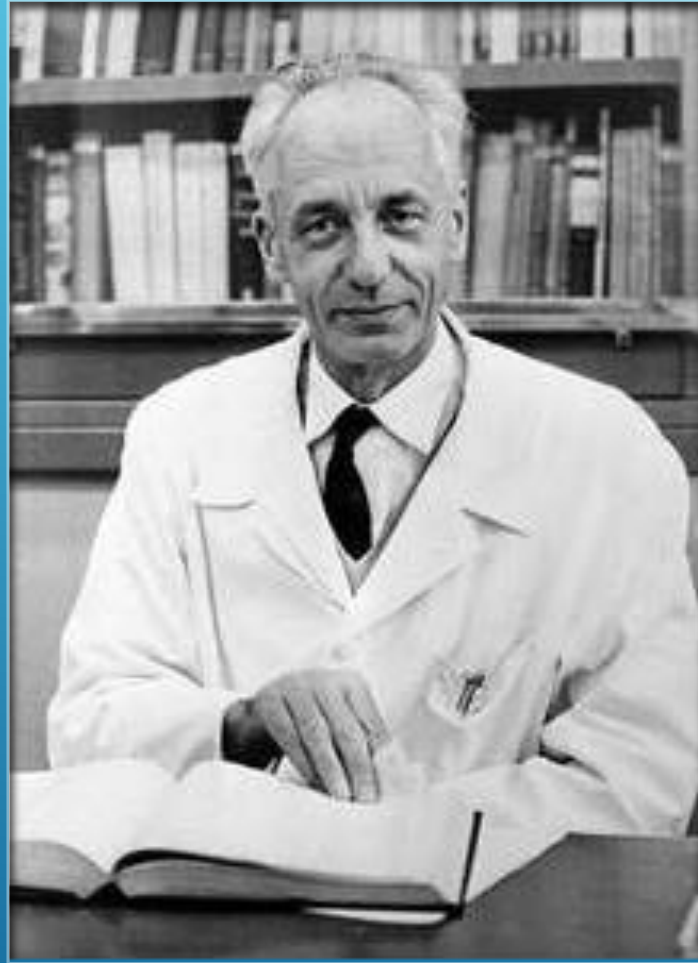




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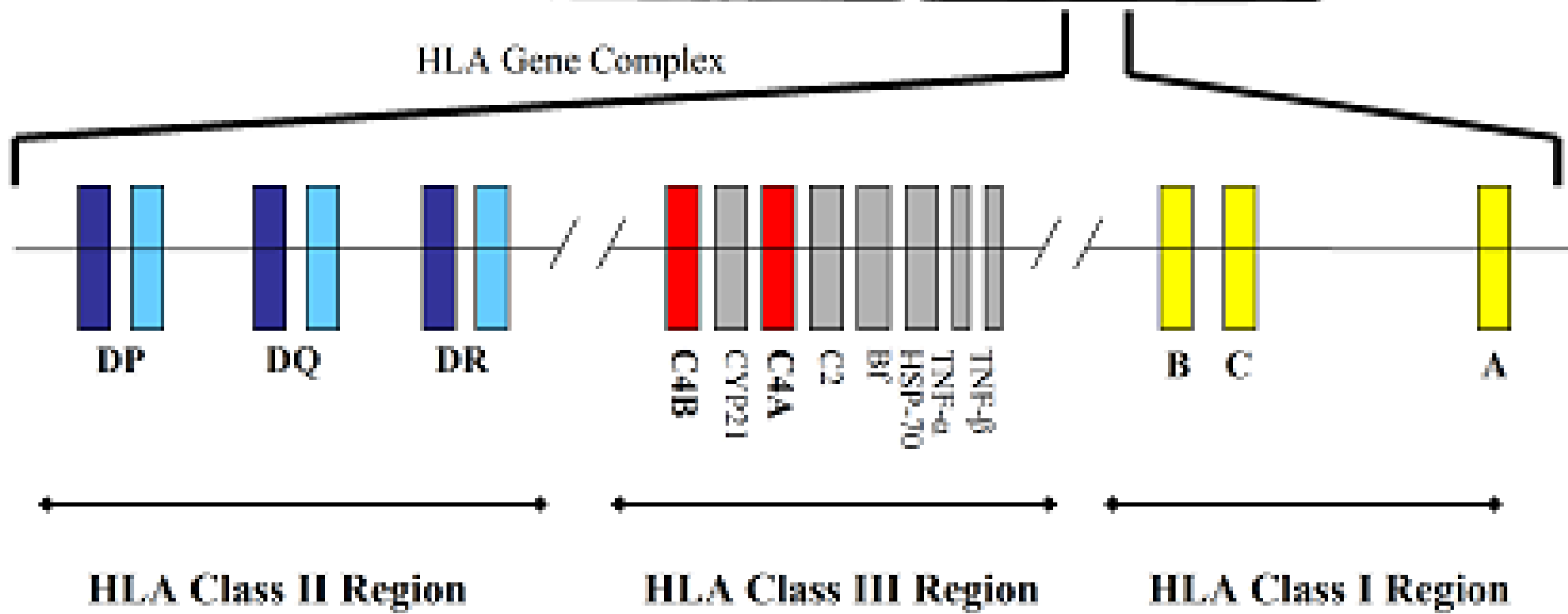
F. LINDBERG 1902



Chromosome 6



HLA Gene Complex





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F. LINDBERG 1902





Lymphocytotoxic cross match test

- ⊙ Panel or donor lymphocytes are incubated with recipient serum in the wells of a microtiter (Terasaki) tray.
- ⊙ followed by the addition of rabbit complement.
- ⊙ After a second incubation period, vital stains (e.g., eosin-y or acridine orange and ethidium bromide) are added, and the wells are viewed using inverted or fluorescent (ultraviolet) microscopy to determine cell viability.



**Acute Rejection, Kidney Allograft
Function, and Graft Survival in
Patients with Circulating Pre-
Transplant IgG Antibodies Directed
Against Donor HLA-A, -B, or -C
Locus Determined Antigens**


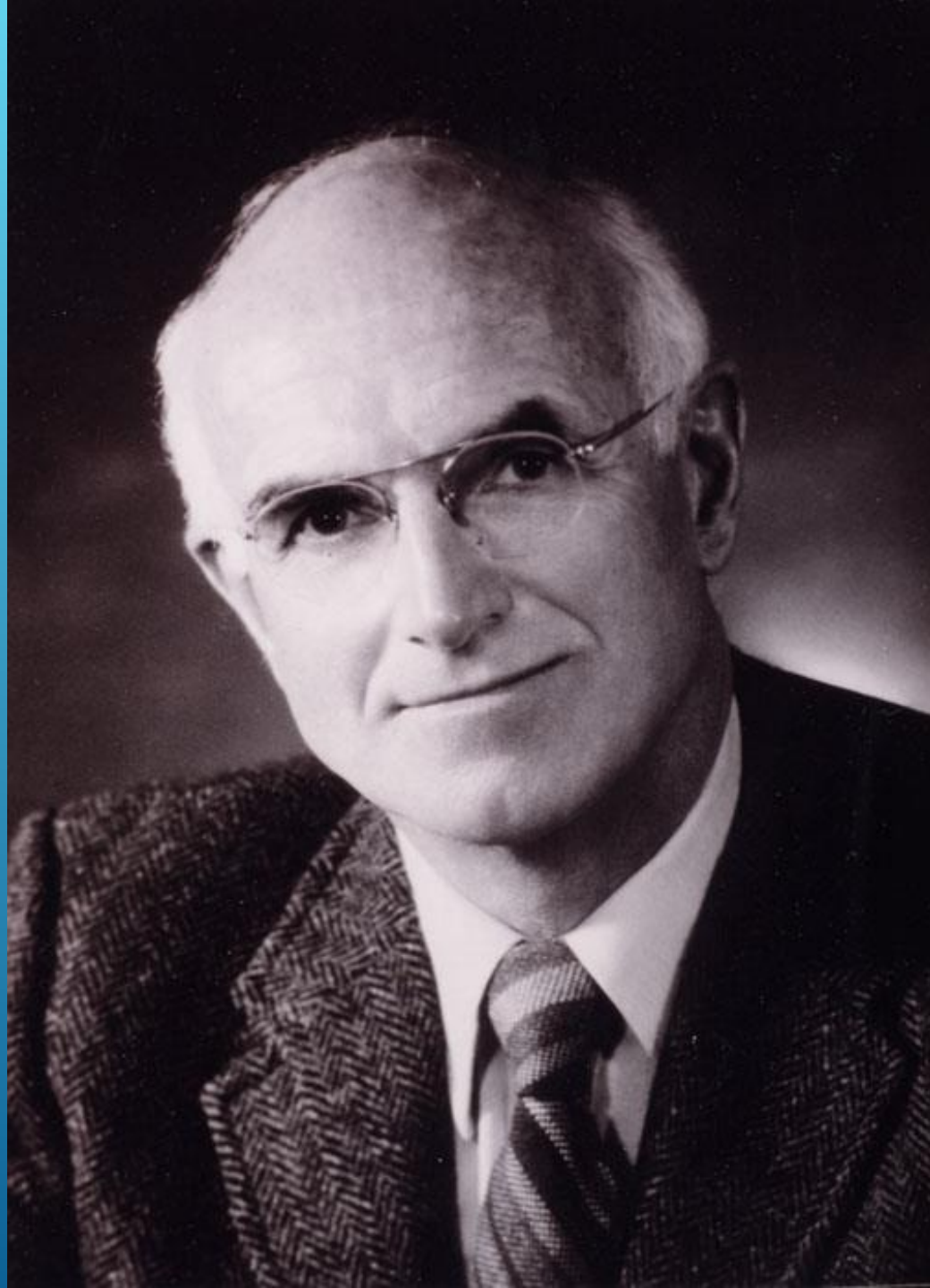




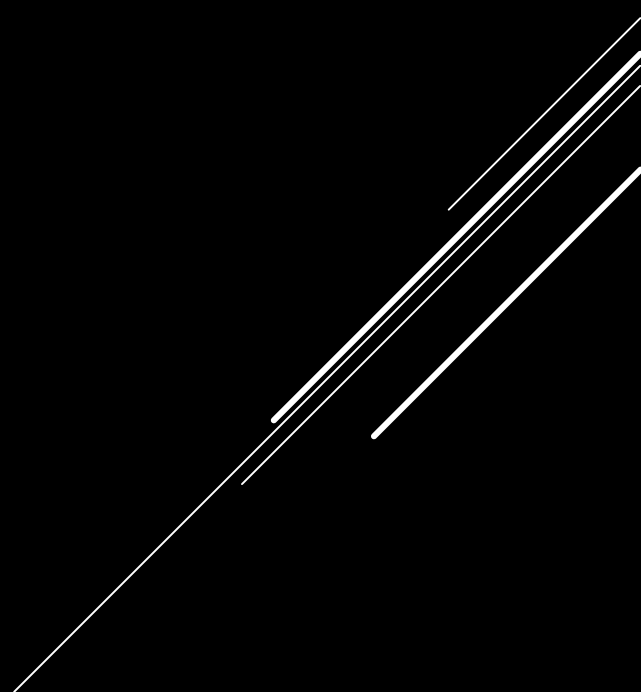
Fig. 1.7 Dr J.E. Murray, Dr J.P. Merrill and Dr J.H. Harrison, who successfully carried out renal transplantation between this set of identical twins on 23 December 1954.







BENT BRIGHAM KIDNEY TRANSPLANT TEAM: CIRCA
rtwell Harrison, John P. Merrill, David M. Hume, Joseph E. Murr



NOBEL PRIZES IN TRANSPLANT

Alexis Carrel 1912 suture blood vessels

FM Burnett

PB Medwar 1960 distinction self vs other

GD Snell

J Dausett

B Benaceraf 1980 MHC

J. Murray

ED Thomas 1990 Organ and cell Transplant





Rejection - More Than the Eye Can See!

*Individualized Management of Kidney
Transplant Recipients*

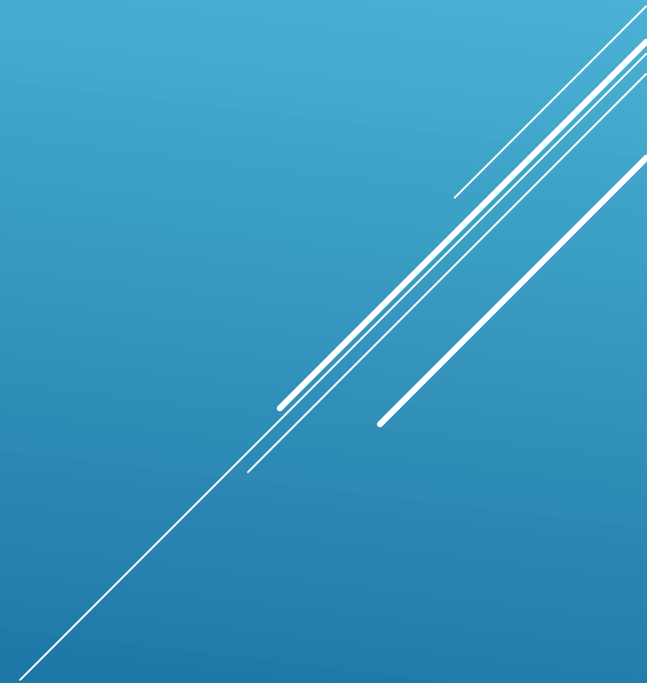
Terry Strom, MD

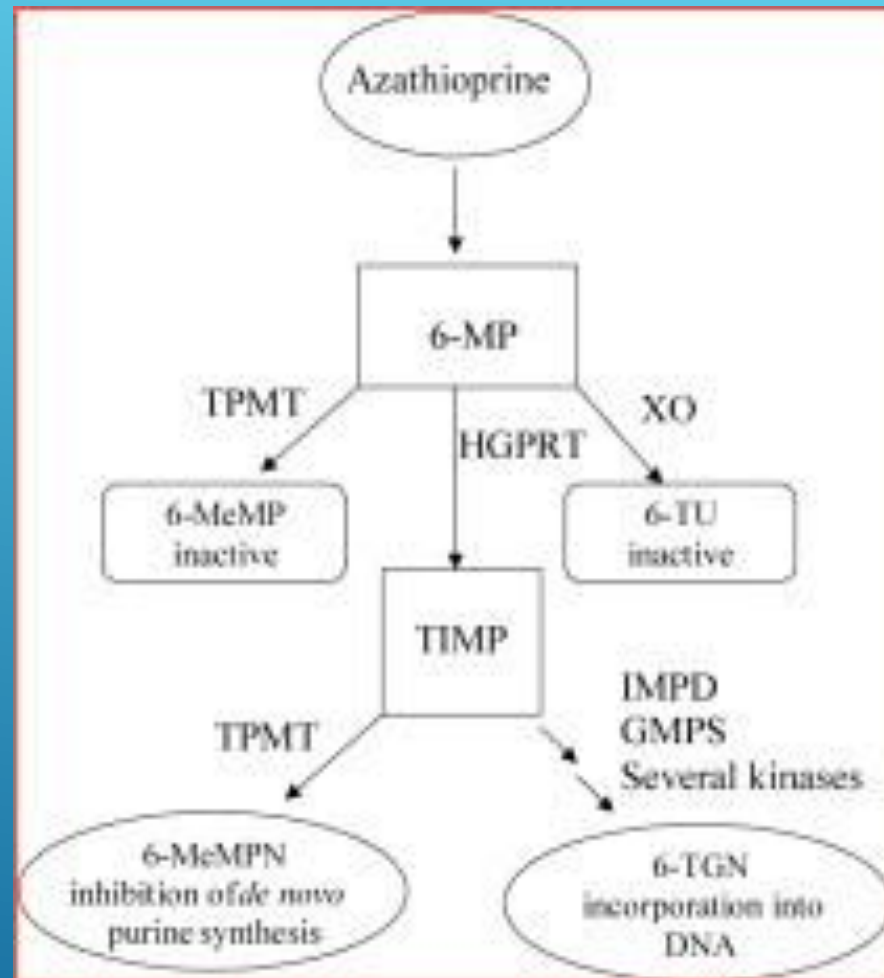
Harvard Medical School

Beth Israel Deaconess Medical Center

Boston, MA 02115

tstrom@bidmc.harvard.edu









ALFR.
NOBEL

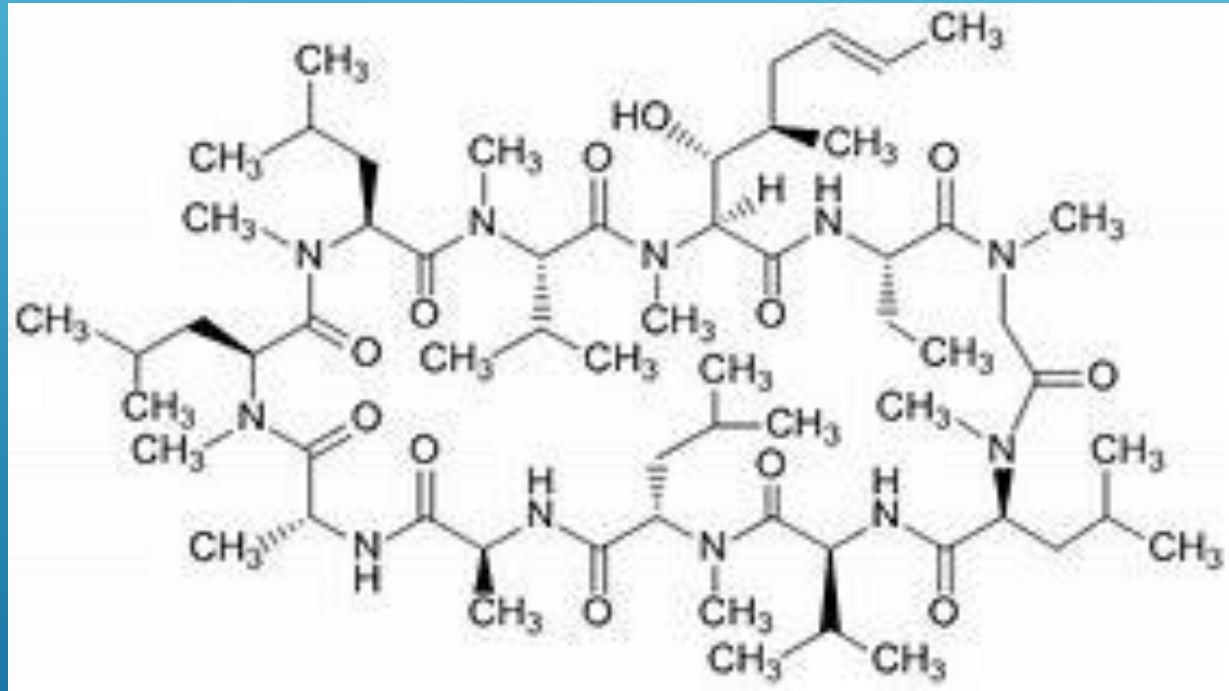
NAT.
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Jean Borel



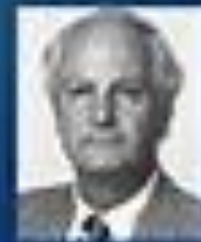




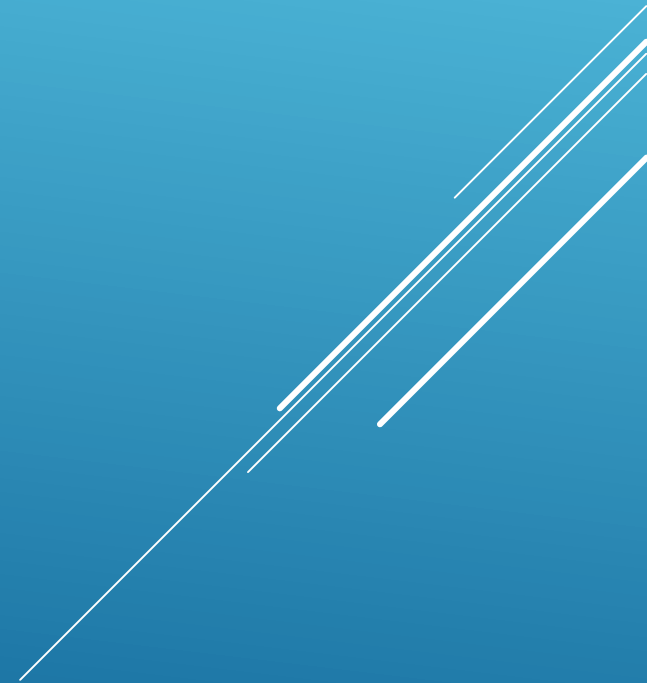
History of Cyclosporine



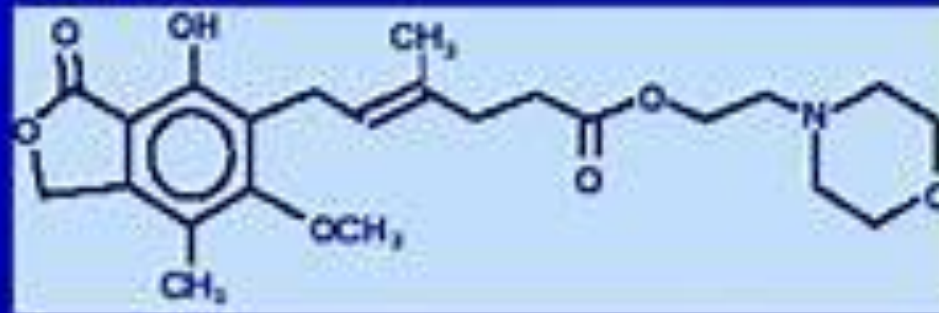
- ▶ Comes from the fungus *Tolypocladium inflatum* which was discovered in 1970.
- ▶ *Tolypocladium inflatum* was isolated from Norwegian soil samples.
- ▶ Found to be immunosuppressant— cyclosporine in 1976 by J. F. Borel
- ▶ Cyclosporine was approved for use in 1983 to prevent graft rejection in transplants.
- ▶ Approved for the treatment of severe psoriasis in 1997.



Anthony C. Allison



Mycophenolate Mofetil

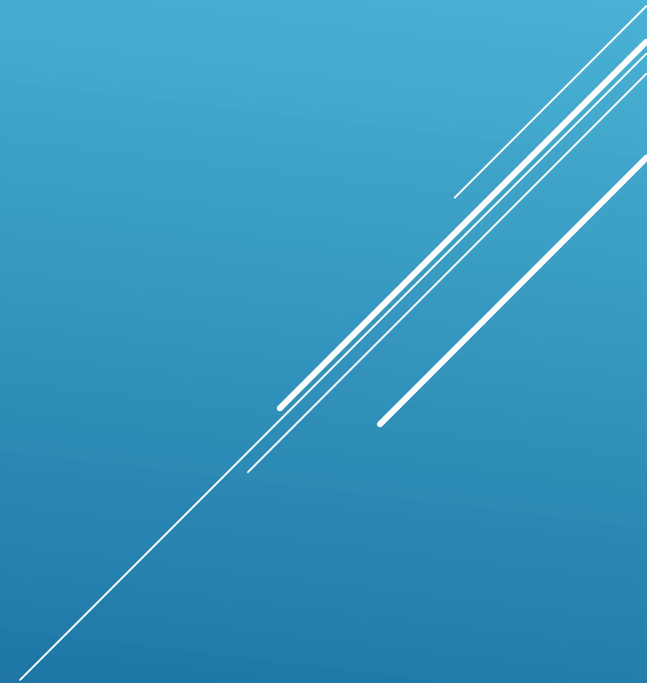


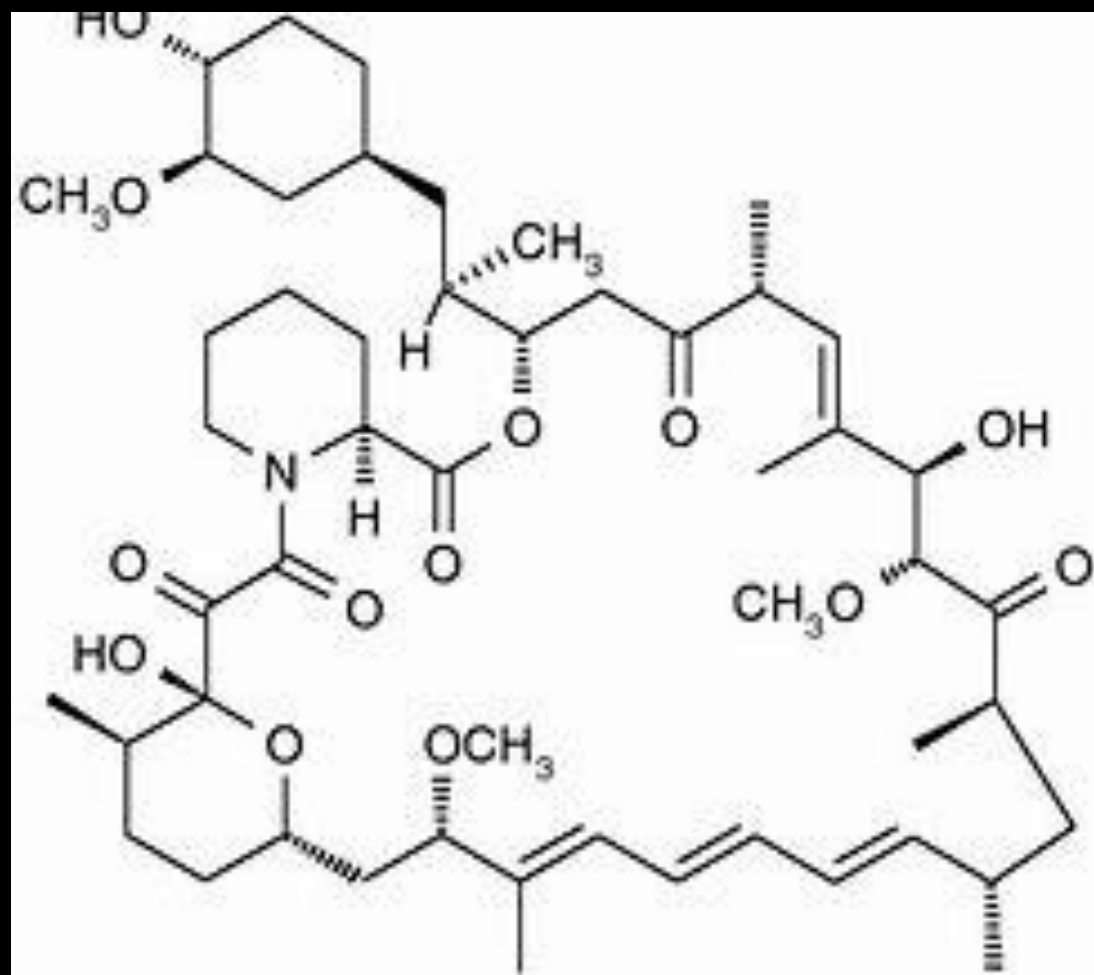
- Ester of MPA (*penicillium* fermentation)
- Antimetabolite: IMPDH / purine synthesis inhibitor
- Lymphocyte-selective (no salvage pathway)
- FDA-approved for kidney transplantation in 1995 and LTX in 2000

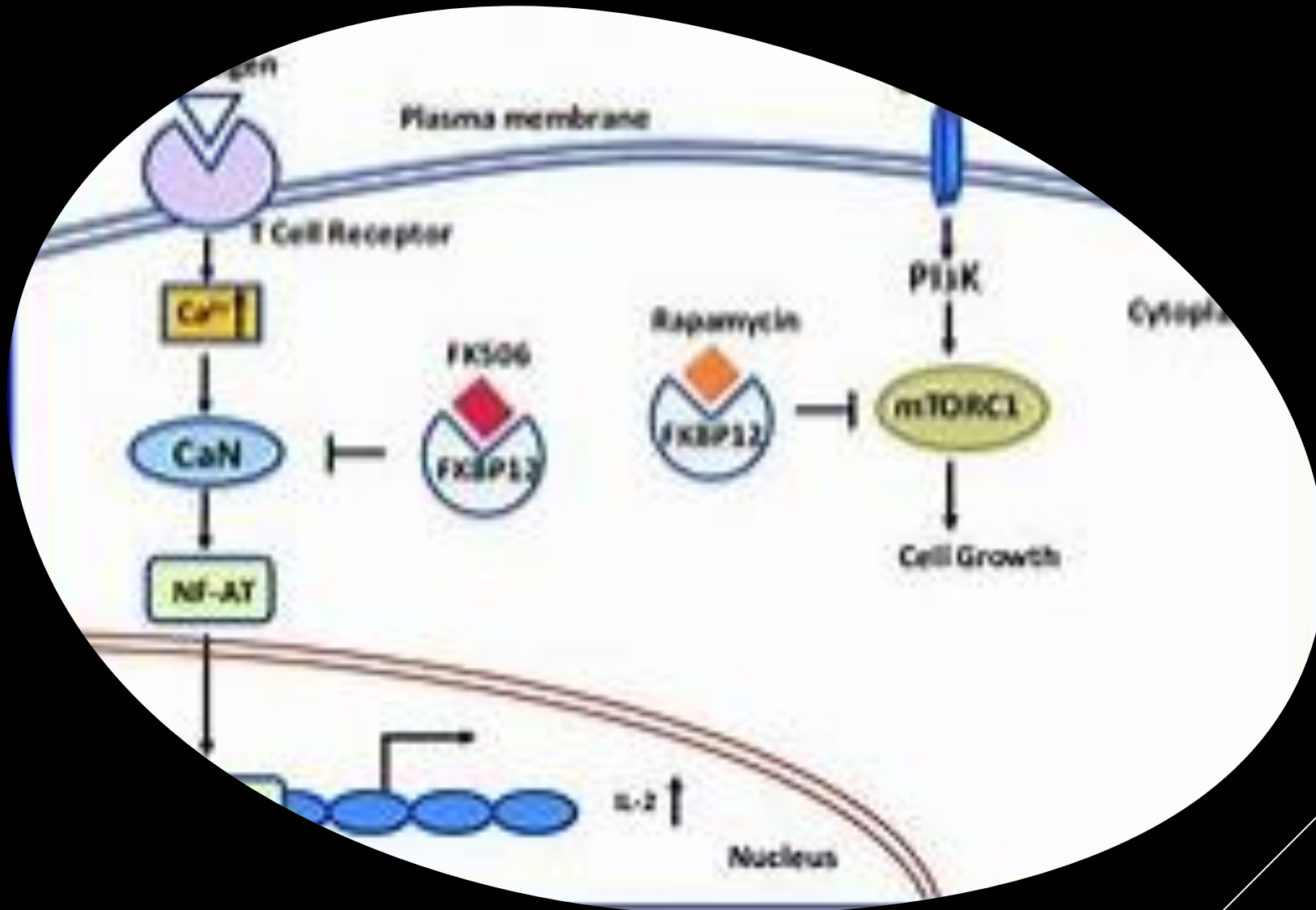
MPA, mycophenolic acid












Transplant science and practice has
Begun as response to **War** , studied in
The **Mouse** leading to new life for
many **Humans** with organ
Failure.

A decorative graphic consisting of several parallel white lines of varying lengths, slanted diagonally from the bottom right towards the top right, set against a blue gradient background.