



divisione di  
paleopatologia



UNIVERSITÀ  
DI PISA



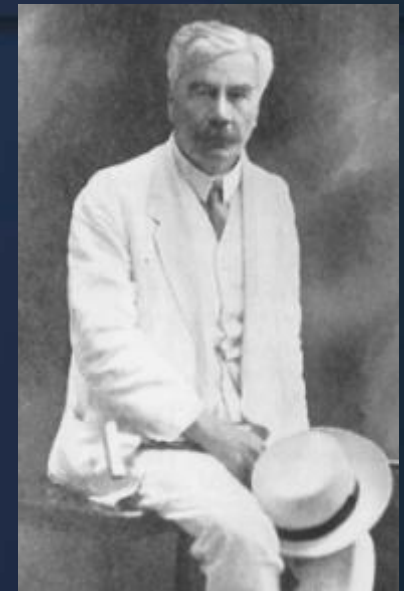
University of Pisa  
Division of Paleopathology,  
History of Medicine and Bioethics

**Gino Fornaciari**

*The challenging case  
of Cardinal Carlo de' Medici*

The First Clinical Challenge:  
Eminence versus Evidence in Spondyloarthritis  
*June 22-23, 2012 – Pisa*

Paleopathology, defined by Sir Armand Ruffer, one of the founders of discipline, – “*the study of disease in ancient human remains*” – diagnoses diseases directly in ancient human bodies, skeletons or mummies.



Sir Armand Ruffer (1859-1917)



### Skeletons

XI century burial,  
Monte di Croce castle, Tuscany)



### Mummies

(Renaissance mummies,  
Basilica of S. Domenico Maggiore, Naples)

**Direct data**

**PALEOPATHOLOGY**

# PALEOPATHOLOGY



**INTEREST**

**Anthropology**



**Life style of ancient  
populations**



(trauma, arthritis..)

**Medicine**

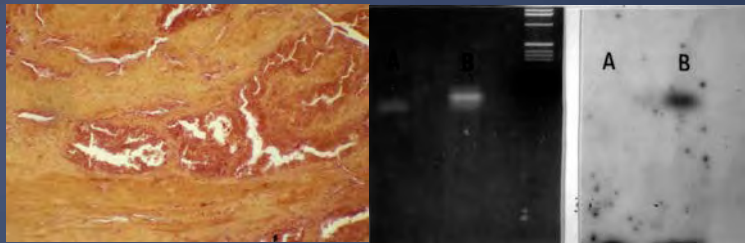


**Origin and evolution  
of diseases**

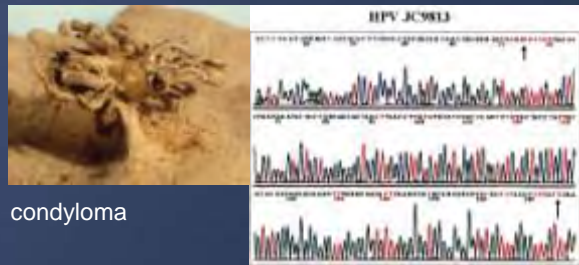


(infectious diseases, cancer..)

# The Paleopathology Group of Pisa University obtained some important results:

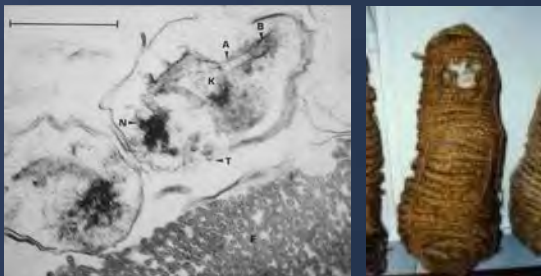


XV century colon cancer, with  
gene K-ras mutation (1996)



condyloma

XVI century HPV virus  
(2003)



XII century American trypanosomiasis  
(1992)



Smallpox virus

XVI century  
smallpox (1986)



*Treponema pallidum*

XVI century venereal  
syphilis (1989)



Malaria and Leishmaniasis of  
the Medici (2011)



The Medici were one of the most powerful families of the Italian Renaissance. Starting from the 14<sup>th</sup> century, their careful management of banking ventures and skilful political actions brought them to the forefront of social and political power in Tuscany and in Florence, the intellectual center of the Western world.

Lovers of art and science, the Medici were patrons of Michelangelo, Leonardo da Vinci, Botticelli, Galileo, and Benvenuto Cellini.



Lorenzo the Magnificent  
(1446-1492)  
Vasari, Uffizi Gallery



Michelangelo  
Tomb of Giuliano de' Medici  
(Medici Chapels, Florence)

# THE “MEDICI PROJECT”



John of the Black Bands  
(1498-1526)



Cosimo I  
(1519-1574)

In 2002, dr. Antonio Paolucci, Superintendent of Florentine Museums, granted permission to examine 49 of the Medici burials in the Basilica. The "Medici Project" focuses on the Grand Dukes, who are less known than Lorenzo and his descendants.

The project involved collaboration among the University of Pisa, the University of Florence, and the Superintendence of Florentine Museums.

The most recent biomedical techniques were employed in order to obtain as much information as possible about the life style, the health and the environment of these famous rulers of Renaissance Florence.

I present here an important case of symmetrical polyarthrititis found in the course of the “Medici Project”.



Eleonora from Toledo  
(1522-1562)



Anna Maria Luisa  
(1667-1743)



The Lorena Chapel

In order to conduct this study, we set up a temporary laboratory in the Lorena Chapel, the funerary crypt of the Grand Dukes of the Lorena dynasty, which ruled Florence and Tuscany after the Medici until 1859.



The temporary laboratory

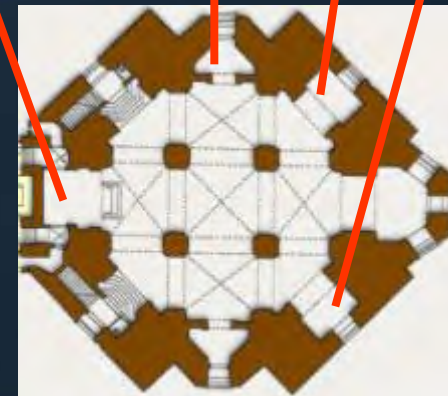


Some anthropologists at work

# THE CRYPT OF SAN LORENZO



The crypt of the Basilica of San Lorenzo in Florence, Mausoleum of the Grand Dukes of the Medici family.



Map of the crypt, with the Medici tombs already explored in yellow.



# THE "RICH" PATHOLOGY OF THE MEDICI FAMILY

(from archive documents)

INFECTIOUS AND  
PARASITIC  
DISEASES

METABOLIC  
DISEASES

JOINT DISEASES

CARDIOVASCULAR  
DISEASES

TUMORS

MALFORMATIONS

smallpox  
tuberculosis  
malaria  
syphilis

obesity  
anemia  
urinary stones

**ARTHRITIS**

arteriosclerosis

breast cancer

dwarfism



Ferdinando II (1610-1670)



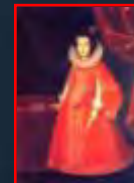
Francesco Maria (1660-1710)



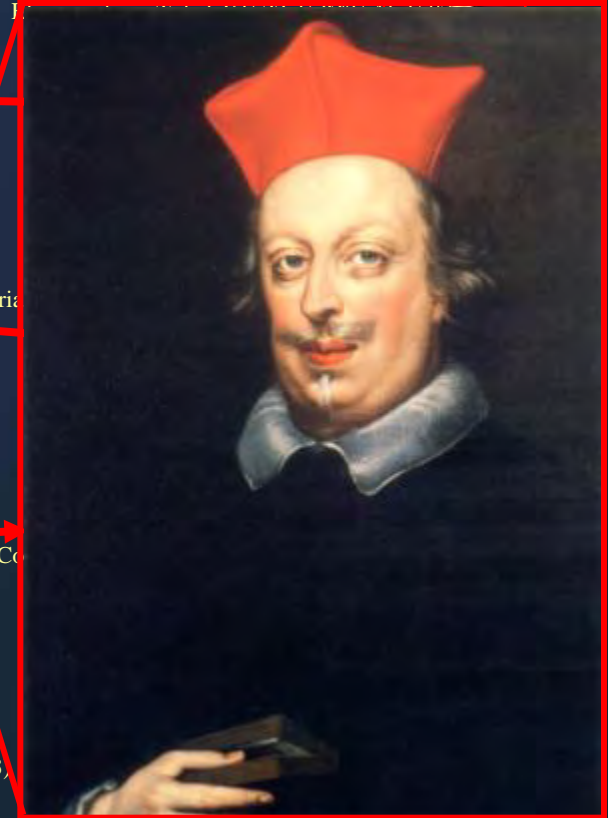
Cardinal Carlo (1596-1666)



Anna Maria Luisa (1667-1743)



Maria Cristiana (1609-1632)



Cardinal Carlo  
(1596-1666)

# Position of the tomb of Cardinal Carlo de' Medici





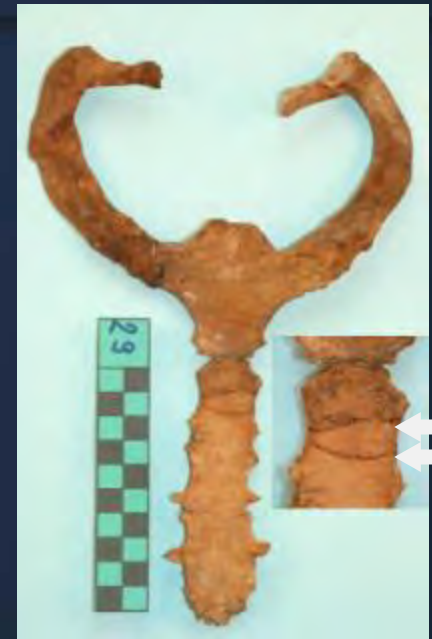
Sustermans (c.1640), Florence

## Cardinal Carlo (1596-1666)

## Anthropology

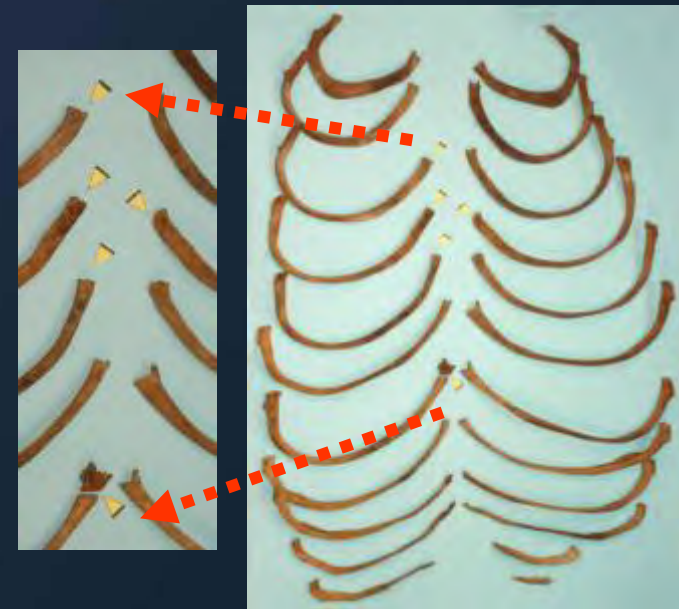
Carlo (1595-1666), younger son of Ferdinand I, became cardinal in 1615 and dean of the Sacred College of Cardinals in 1652.

His skeleton is that of a senile man aged more than 60 years, 1.70 m tall, with severe osteoporosis, especially of the lower limbs.



## Autopsy

There are two transversal cuts on the upper part of the sternum (blue arrows); the sternal extremities of the 4<sup>th</sup>, 5<sup>th</sup>, 6<sup>th</sup> and 8<sup>th</sup> right ribs, and the 5<sup>th</sup> of the left, appear completely sectioned (red arrows), probably with scissors.



## “Clinical history”

We know that, at 8 years of age, he was affected by **tuberculosis of the column** (Pott's disease), upper thoracic or cervical.

From 24 years of age he suffered from an **acute articular disorder** of the feet, hands and knees, diagnosed as 'gout' by the physicians;

the documents report on **18 severe attacks** from the ages of 35 to 59, with **worsening between 60 and 65**.

From the ages of 50 to 70 he was affected by recurrent bronchitis and finally died of bronchopneumonia.



Sustermans (c.1650), Florence, Palatina Gallery

# Paleopathology

The facial skeleton shows a marked **hypoplasia of the right mandibular corpus**, with right deviation of the face and probable chronic *torticollis*, as appears in a rare engraving (white arrow).



Haelvegh, engraving



X-ray Prof. N. Villari  
(University of Florence)

A block, involving the vertebral bodies with wedge-shaped collapse, fusion, and formation of an angular kyphosis (green arrows), is at the level of C6-C7.

X-ray confirms body fusion (green arrows).



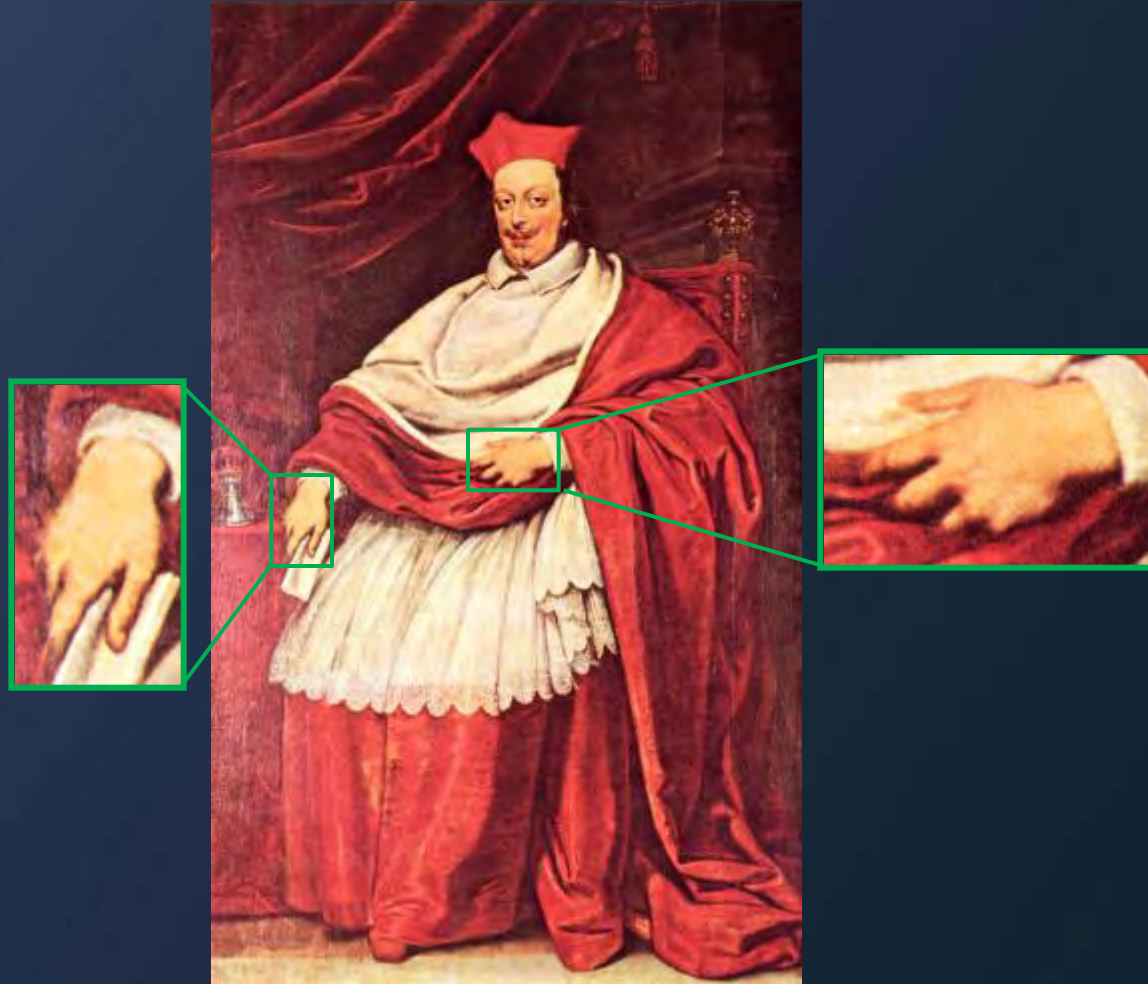
There is also diffused periostitis of the internal surface of the ribs (blue arrows), typical of tuberculosis.



These are the results of the cervical spine tuberculosis (Pott's disease), characterized by neck *fistula* and *gibbus*, well described in the archival records, at 8 years of age.

## “The portraits”

The portraits, at about 60 years of age, show **symmetrical, severe arthropaty** of the hands, with evident deformity and atrophy of 1<sup>st</sup>, 4<sup>th</sup> and 5<sup>th</sup> finger of the left hand.



Sustermans (c.1650), Florence, Palatina Gallery

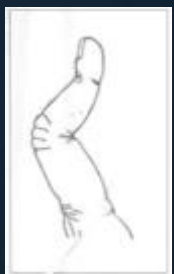
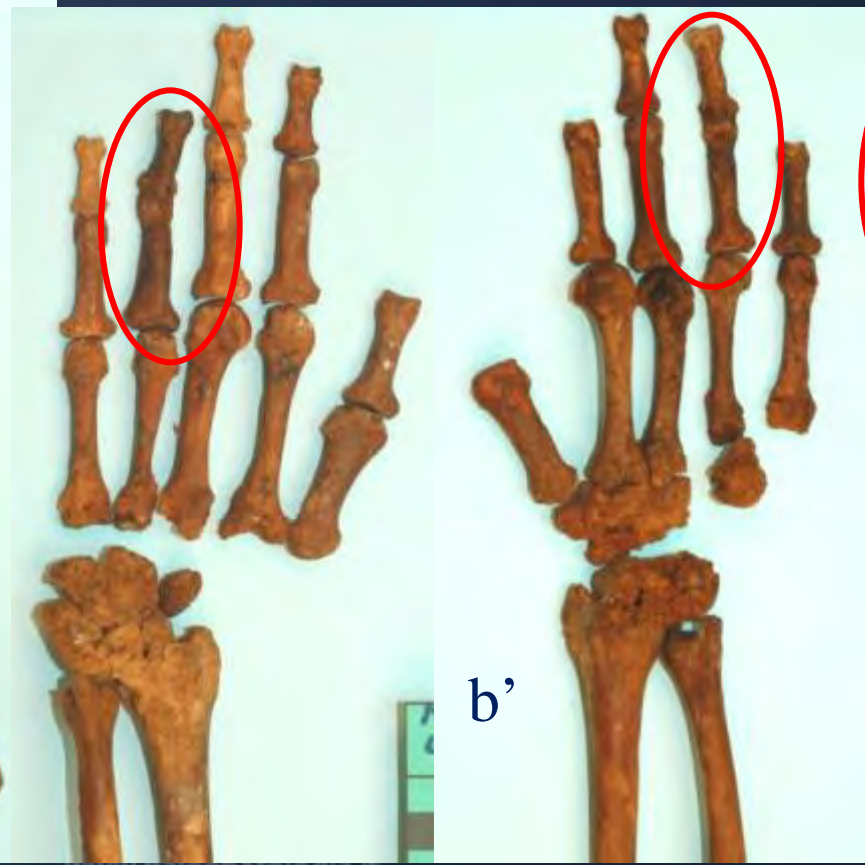


The post-cranial skeleton shows an ankylosing disease, symmetrical and extremely severe, of the great and small articulations, characterized by:

- Fusion of the elbow (in flexion at 55°) (a, a');



- Bilateral fusion of wrists, carpal bones, and some fingers (b, b'), with bilateral swan-neck deformity (c).



- Fusion of the right sacroiliac joint (d)  
(red arrow)



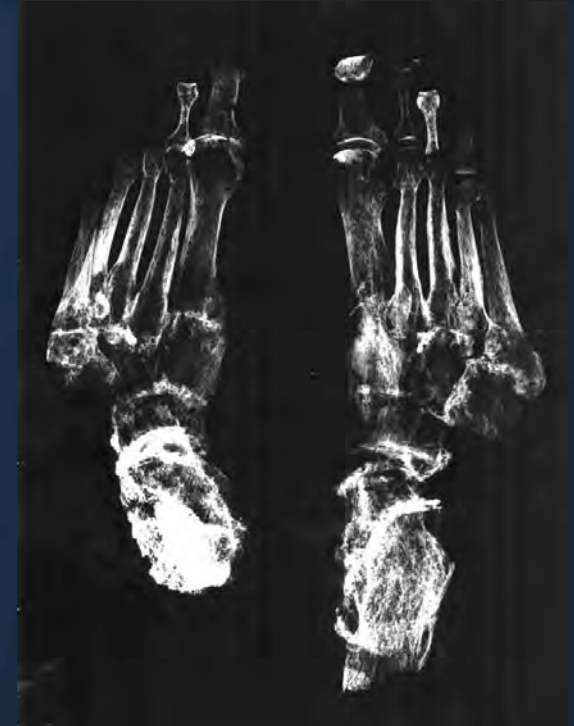
- Fusion of knees and *rotulae*  
(in flexion at 90°) (e)



X-ray Prof. N. Villari  
(University of Florence)



- Fusion of tarsal and metatarsal bones (f)



X-ray Prof. N. Villari  
(University of Florence)

This data, together with the very severe osteoporosis, in particular of the lower limbs, demonstrates the cardinal's total disability, in the last years of life, as reported by the archival documents. Indeed, from 1658 (at the age of 63), the cardinal was no longer able to sign any letters or documents. In a letter to a nephew he writes: *“Y(our) H(ighness) please excuse me for not being able to sign in my own hand (writing), because my hand does not function”*

(4 December 1658)

Results of the PCR-SSP genotyping test for **HLA-DRB** locus of Cardinal Carlo:

The band positions of PCR products at *lines 8* and *23* correspond to

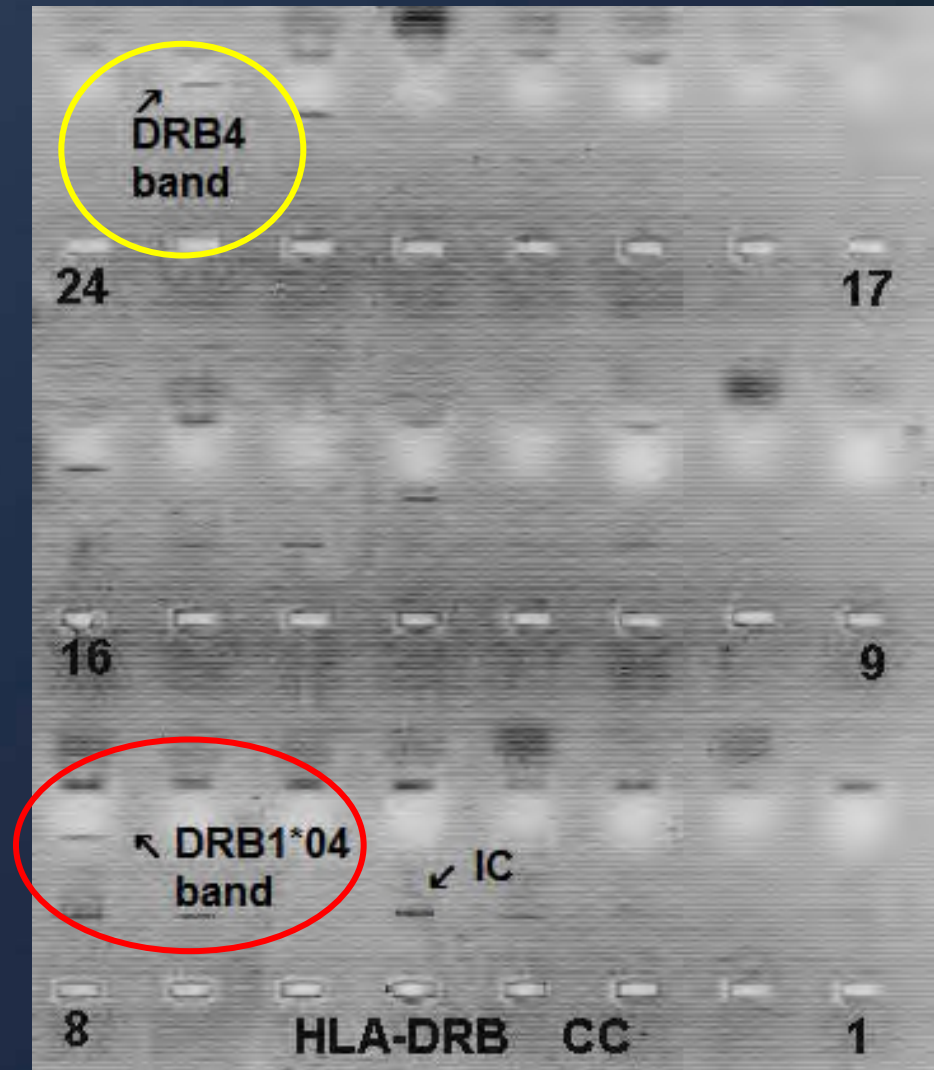
**DRB1\*04**

**DRB4**

alleles

(*Line 1* represents the negative control).

The remaining positive bands define the second alleles of Cardinal Carlo, exactly DRB1\*11 (serotype DR11, *lines 13* and *16*) always co-expressed in conjunction with DRB3 (serotype DR52, *line 22*).



Dr. G. Fontecchio,  
Regional Centre for Immunohematology and Tissue Typing,  
San Salvatore Hospital, L'Aquila

Results of the PCR-SSP  
genotyping test for **HLA-C** locus  
of Cardinal Carlo:

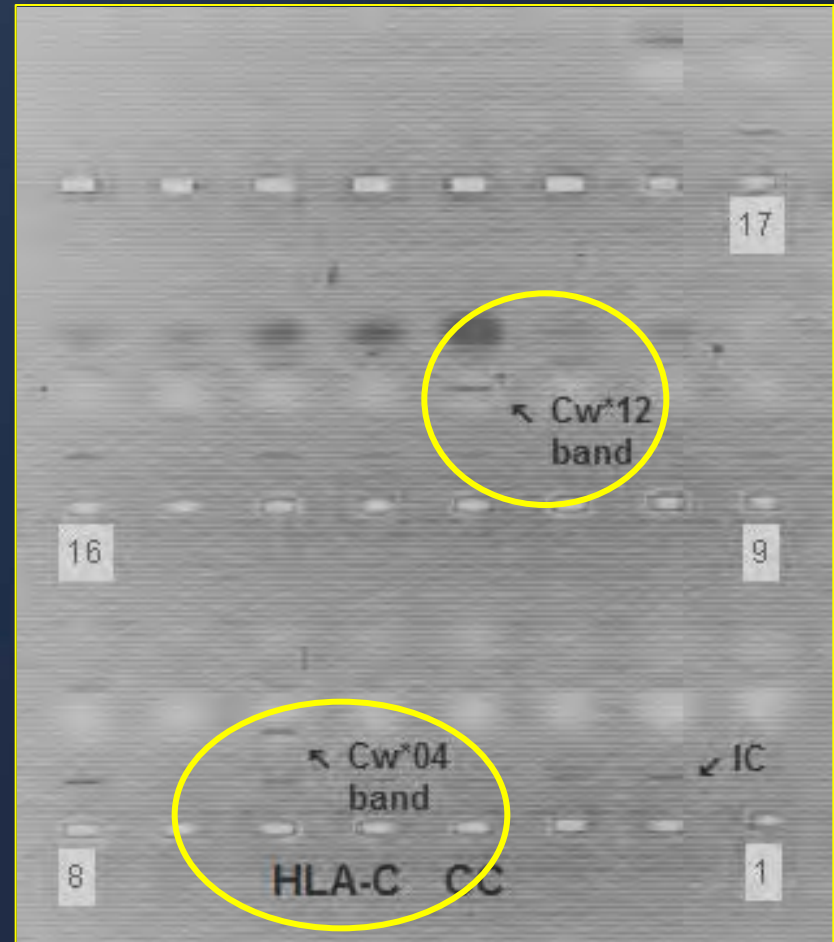
The band positions of PCR  
products at *lines 6* and *12*,  
correspond to

**Cw\*04**

**Cw\*12**

alleles.

(*Line 1* represents the negative control).



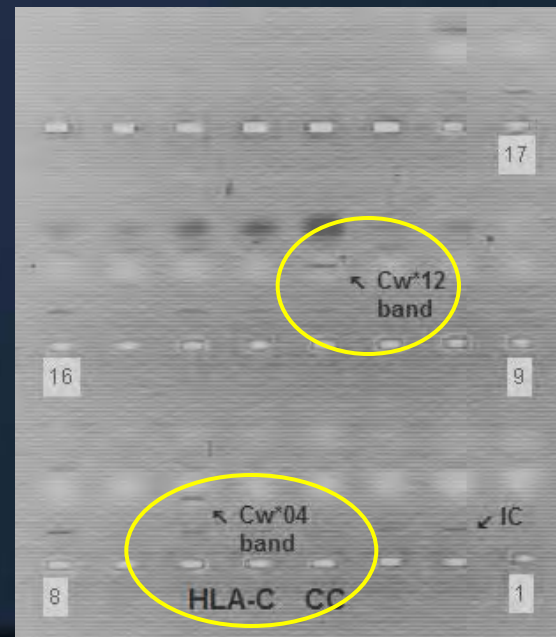
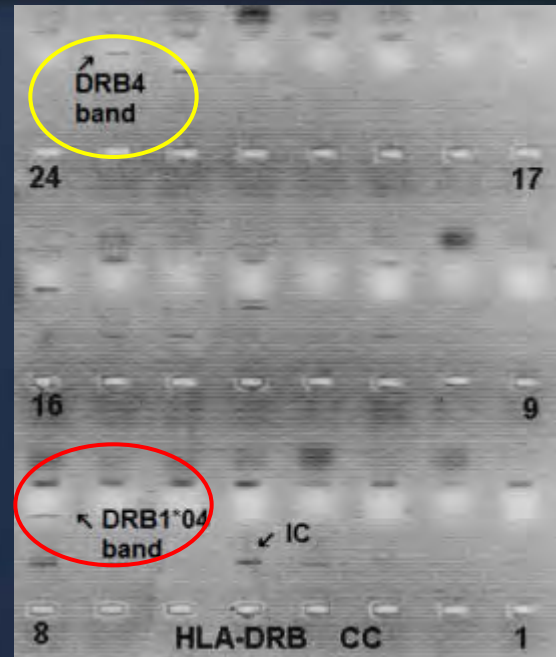
Dr. G. Fontecchio,  
Regional Centre for Immunohematology and Tissue Typing,  
San Salvatore Hospital, L'Aquila

The genotype of Cardinal Carlo de' Medici for the DRB1 and C loci was

**DRB1\*04**/\*11 and (**Cw\*04**/\*12).

He was bearing the specificity **HLA-DR4** predisposing to **Rheumatoid Arthritis (RA)**, but **not HLA-Cw6**, the strongest risk factor for **Psoriatic Arthritis (PsA)** and Psoriasis.

The DRB1\*11, Cw\*04 (Cw4 in serology) and Cw\*12 alleles are not involved in the onset of RA, PsA or other rheumatic diseases.





Possible terminal “clinical picture” of the Cardinal  
(from Pasero, Marson , 2006)

The “clinical”, pathological and molecular picture clearly shows severe **rheumatoid arthritis (RA)**, excluding psoriatic arthritis characterized by similar, but not identical, macroscopic lesions.



## **Institutions involved**

**University of Pisa**

**Superintendence of Florentine Museums**

**University of Florence**

**Opificio delle Pietre Dure**

**Opera Mediceo-Laurenziana**

**University of Long Island**

**University of Minnesota**

**MGM Biotechnology, Pisa**

