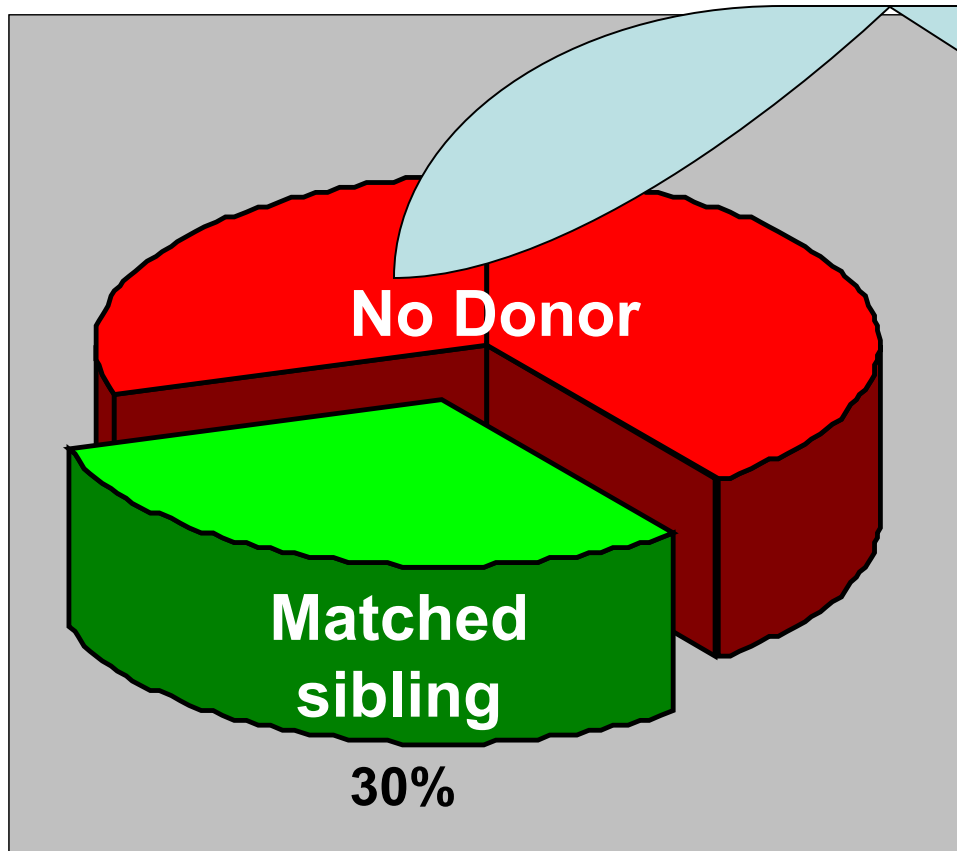


Alta Tecnologia e Ricerca

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PROBABILITY OF HAVING A BONE MARROW DONOR



HSCT from an
alternative donor
is the only option

- matched unrelated donor
- unrelated cord blood unit
- mismatched family donor

Matched unrelated donor HSCT

Disadvantages

- **30-40 % of patients do not find a matched donor**
- **Many high-risk acute leukemia patients who might find an appropriate donor often relapse while the HLA typing is in progress or while waiting to start the transplant procedures**
- **More accurate matching inevitably reduces the probability of identifying a suitable donor**
- **Other drawbacks:**
 - Age > 50 yrs , advanced stage disease**

UNRELATED CORD BLOOD TRANSPLANT

Advantages

Median search time <1month

Rare haplotypes 20%

Low incidence of GvHD

HLA mismatches

No risk to donor

Disadvantages

Low stem cell dose

★ Slow hematological recovery

★ High risk of graft rejection in adults

Risk of congenital disease

Naïf status of cord blood lymphocytes

ONE HAPLOTYPE MISMATCHED HSCT

Obvious Advantages

a family donor for almost every patient
no undue delay

Obstacles

T-replete BMT



**High incidence
of severe GvHD***

*mediated by the high
frequency of anti-host
alloreactive T cells
in unmanipulated grafts

T-depleted BMT



**High incidence
of rejection***

*mediated by residual
anti-donor CTL-p's
which survive the
conditioning

Translational Research In Haplo Transplant

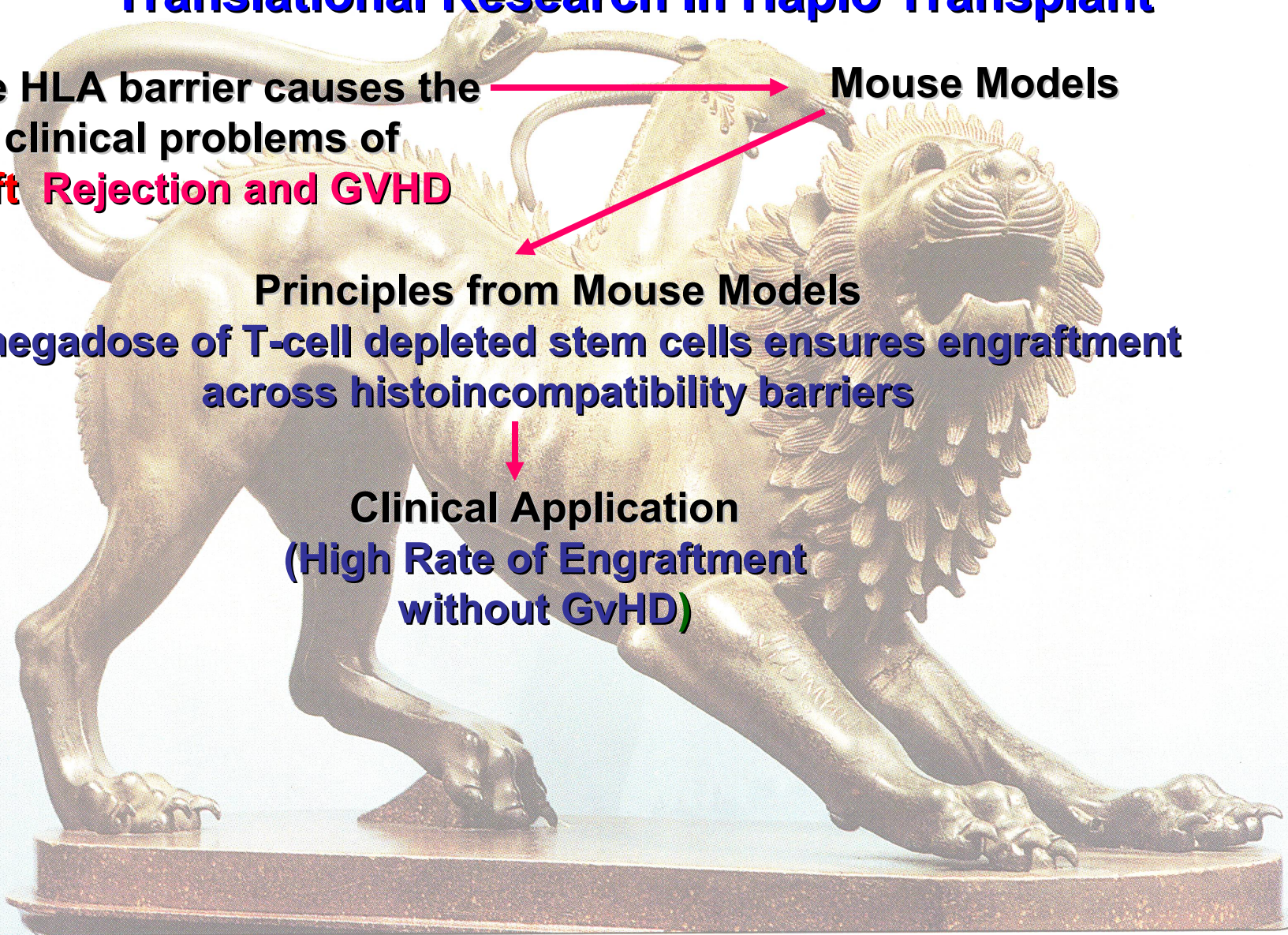
The HLA barrier causes the
clinical problems of
Graft Rejection and GVHD

Mouse Models

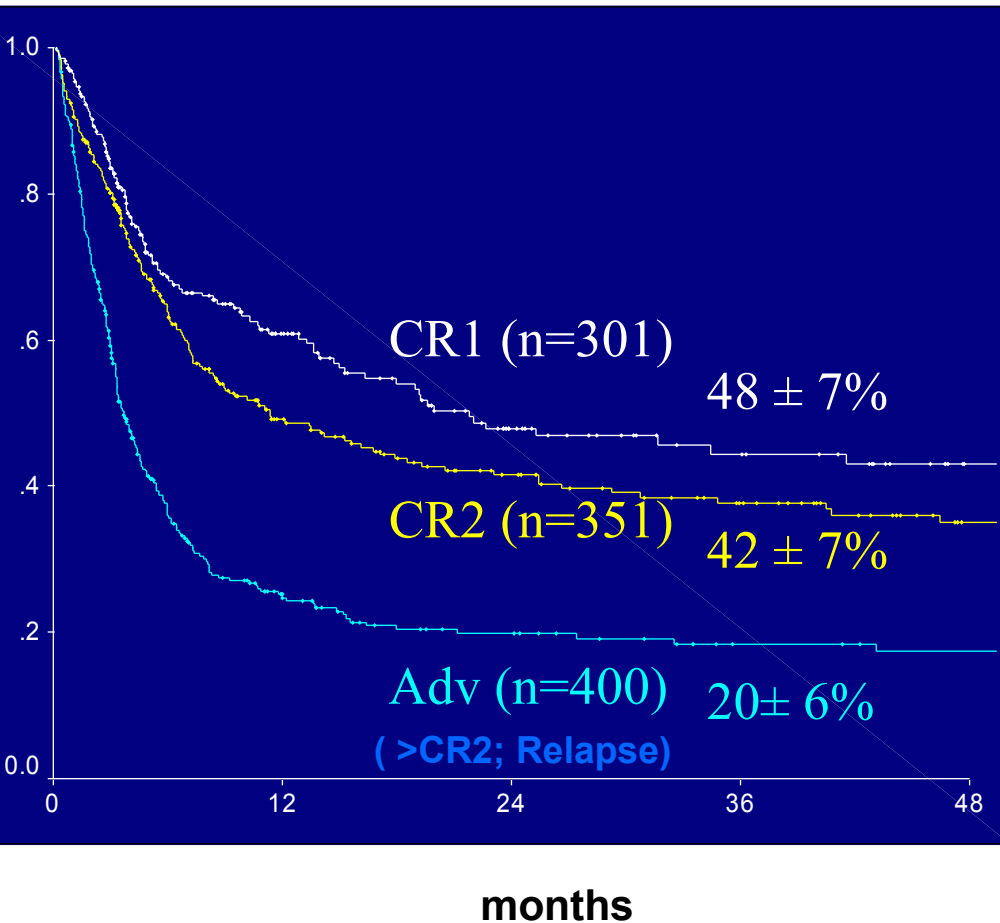
Principles from Mouse Models

**a megadose of T-cell depleted stem cells ensures engraftment
across histoincompatibility barriers**

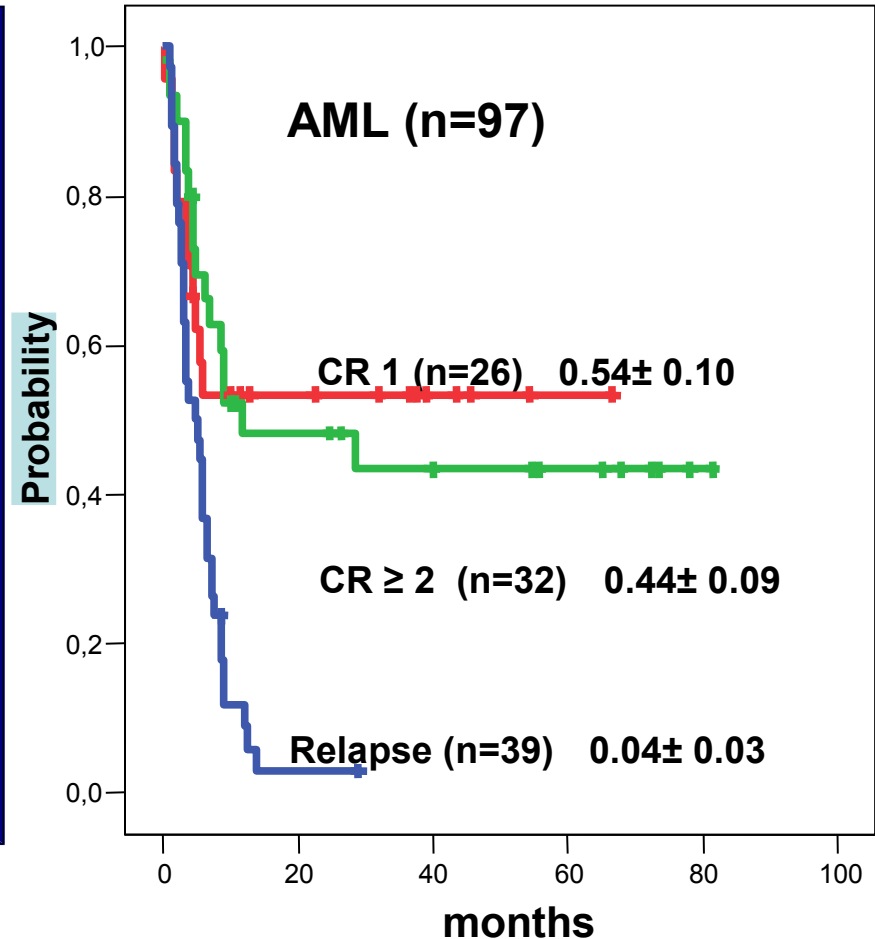
**Clinical Application
(High Rate of Engraftment
without GvHD)**



MUD Transplants in AML Leukemia Free Survival ALWP Study (1922-2002)



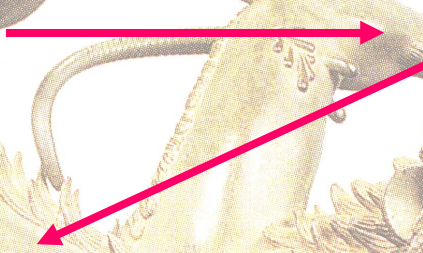
Haplo Transplants in AML Event Free Survival Perugia Study(1999-2005)



Translational Research In Haplo Transplant

The HLA barrier causes the clinical problems of **Graft Rejection and GVHD**

Mouse Models

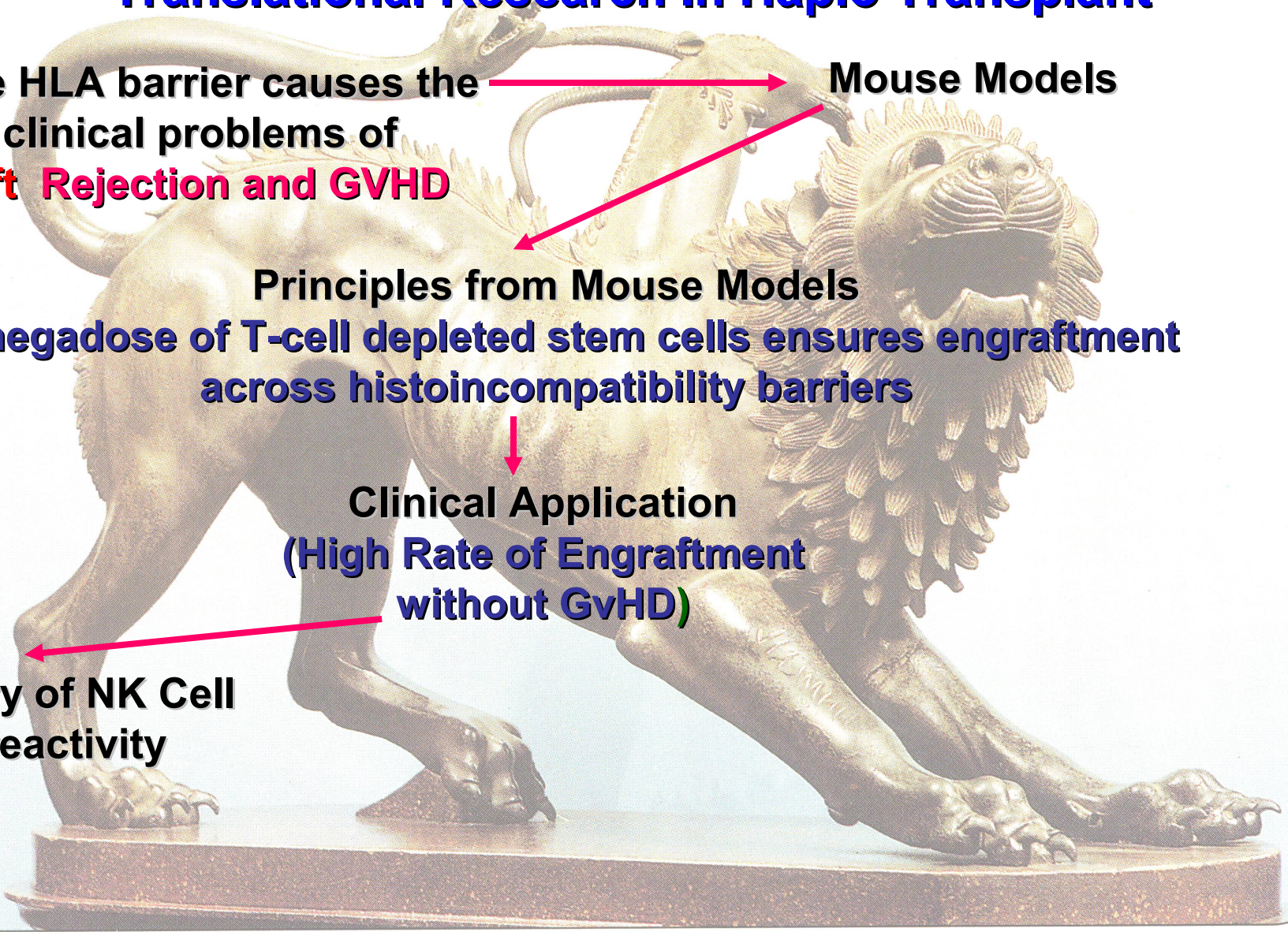


Principles from Mouse Models
a megadose of T-cell depleted stem cells ensures engraftment across histoincompatibility barriers

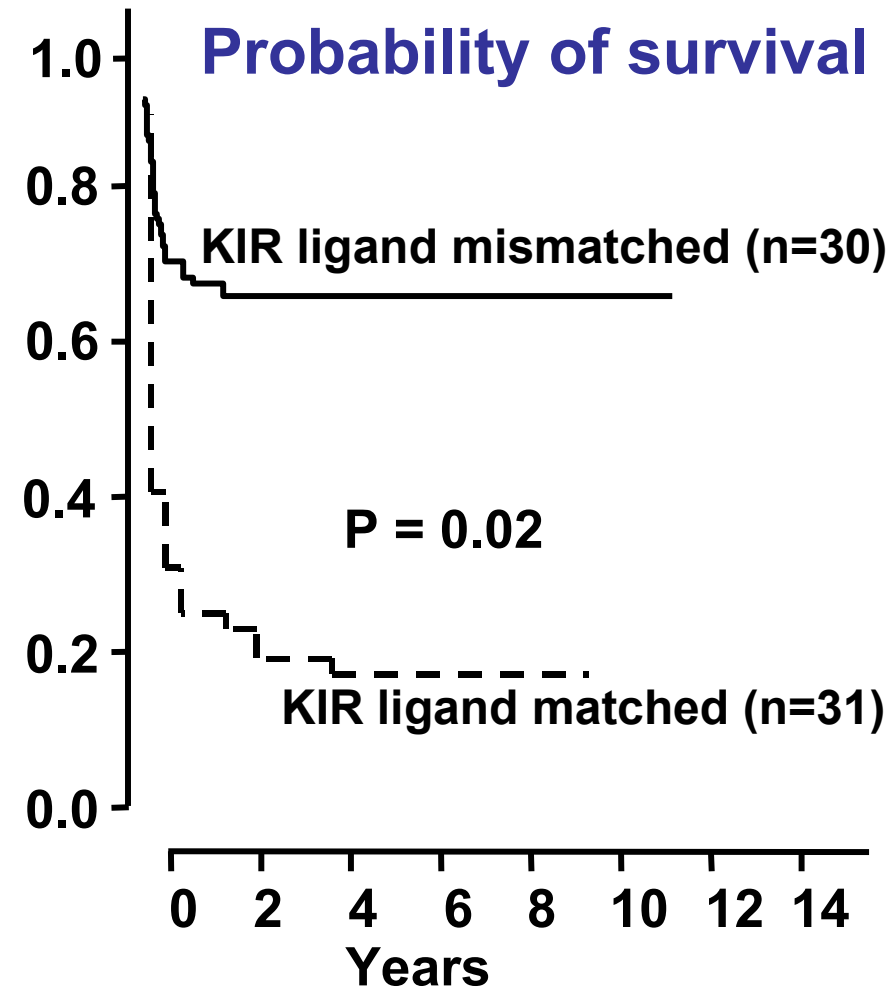
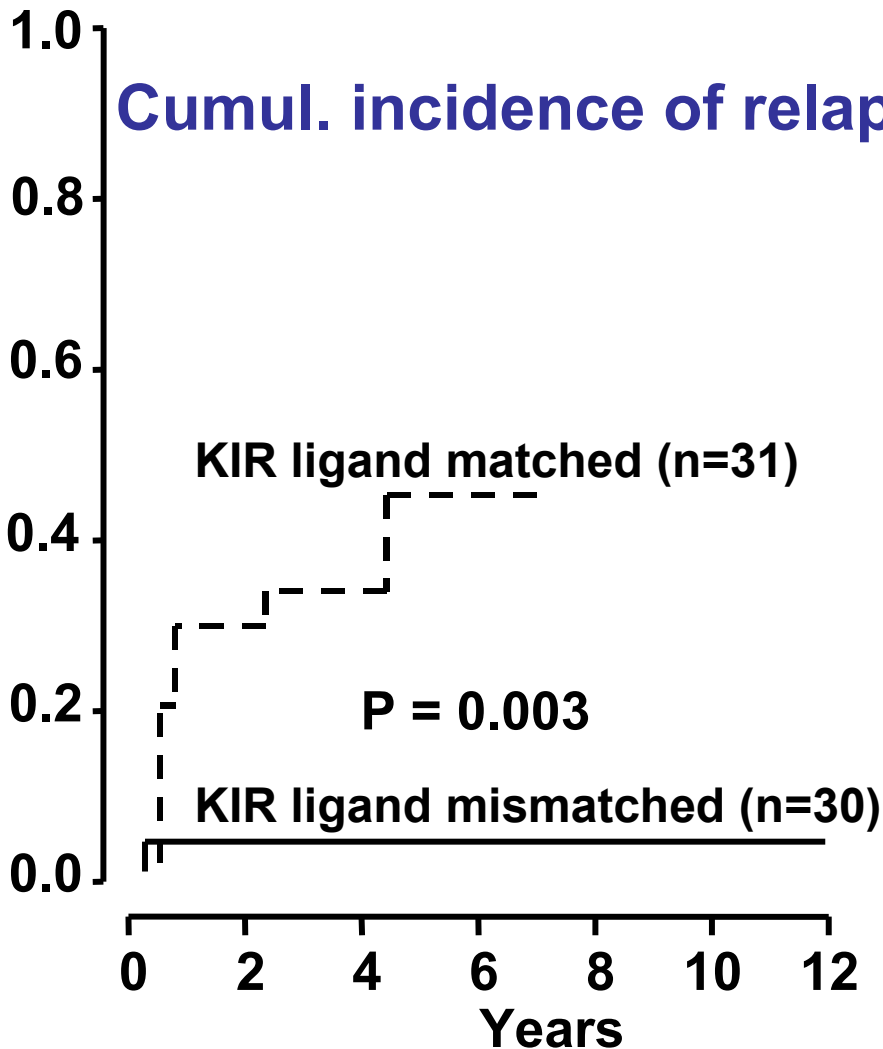
Clinical Application
(High Rate of Engraftment without GvHD)



Discovery of NK Cell Alloreactivity



Relapse and survival of AML patients transplanted in any remission. 1993-2006



Translational Research In Haplo Transplant

The HLA barrier causes the clinical problems of **Graft Rejection and GVHD**

Mouse Models

Principles from Mouse Models
a megadose of T-cell depleted stem cells ensures engraftment across histoincompatibility barriers

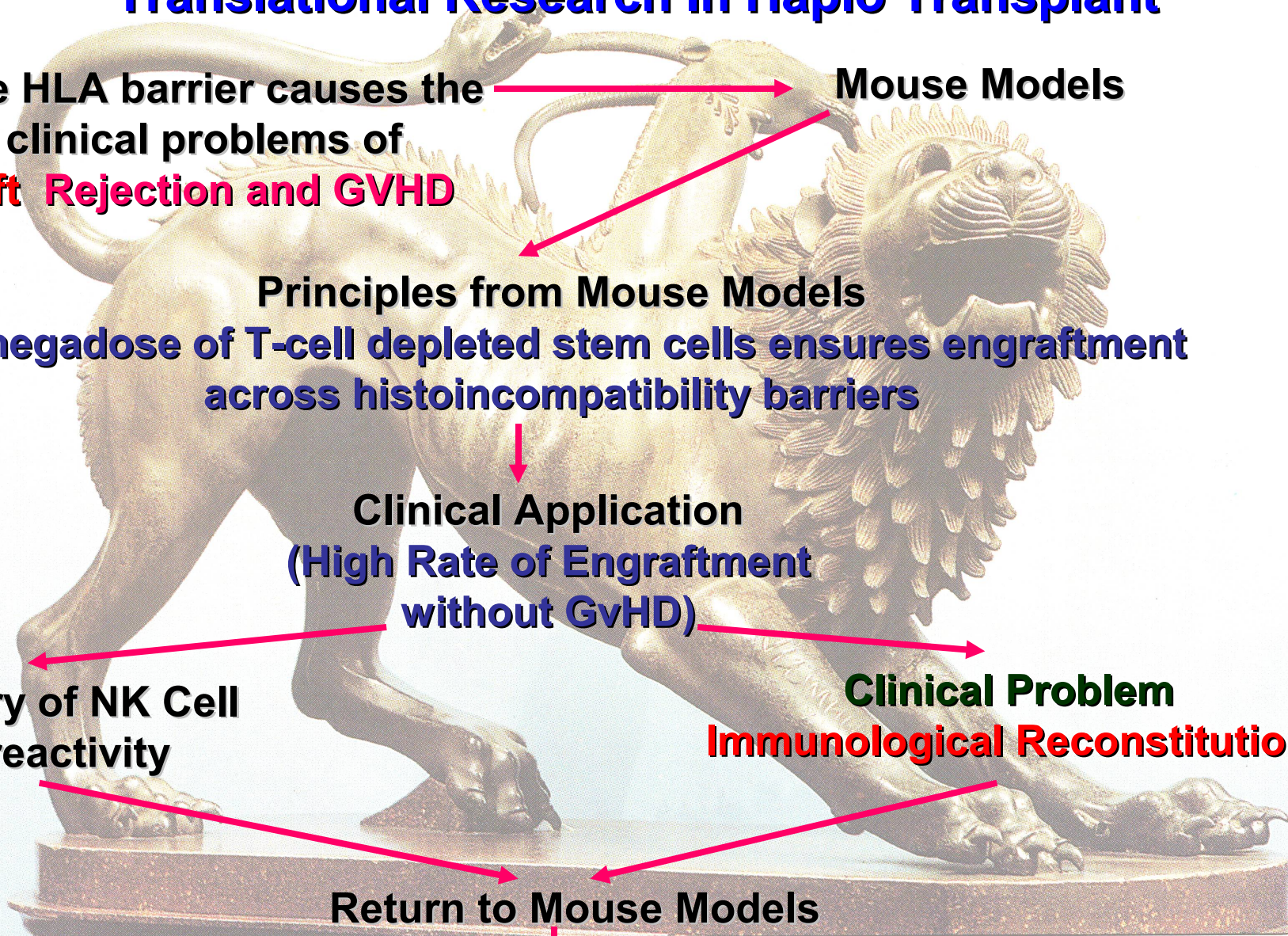
Clinical Application
(High Rate of Engraftment without GvHD)

Discovery of NK Cell Alloreactivity

Clinical Problem
Immunological Reconstitution

Return to Mouse Models

Clinical Exploitation of Principles



ORIGINAL ARTICLE

Cytoplasmic Nucleophosmin in Acute Myelogenous Leukemia with a Normal Karyotype

Brunangelo Falini, M.D., Cristina Mecucci, M.D., Ph.D., Enrico Tiacci, M.D., Myriam Alcalay, M.D., Ph.D., Roberto Rosati, Ph.D., Laura Pasqualucci, M.D., Roberta La Starza, M.D., Ph.D., Daniela Diverio, M.D., Emanuela Colombo, Ph.D., Antonella Santucci, M.D., Barbara Bigerna, Roberta Pacini, Alessandra Pucciarini, Ph.D., Arcangelo Liso, M.D., Marco Vignetti, M.D., Paola Fazi, M.D., Natalia Meani, Ph.D., Valentina Pettrossi, Ph.D., Giuseppe Saglio, M.D., Franco Mandelli, M.D., Francesco Lo-Coco, M.D., Pier-Giuseppe Pelicci, M.D., Ph.D., and Massimo F. Martelli, M.D.,
for the GIMEMA Acute Leukemia Working Party*

LEUKAEMIA

Space shuttle

NATURE REVIEWS | **CANCER** | VOLUME 5 | MARCH 2005 | **157**



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- Liso A., et al., **Leukemia**, 2007 (in press).



AUTOCARRI
IN
MANOVRA

ATTENZIONE

