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التوثيق الالكتروني والميكروفيلم

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بعض الوثائق الأصلية تالفة

Anti-HLA antibodies production and nitric oxide level in the serum and urine of post renal transplant patients in relation to renal graft function and survival.

Thesis

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By

Mohamed Said Abdel Salam

(MBBCh, Alex)

Faculty of medicine

University of Alexandria

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Supervisors

Prof. Dr. Hayam Abdel Meguid El Aggan

Professor of internal medicine

Faculty of medicine

University of Alexandria

Dr. Amel Fouad Ketat

Assistant professor of medical biochemistry

Faculty of medicine

University of Alexandria

Dr. Sherif Aziz Zaki

Lecturer of internal medicine

Faculty of medicine

University of Alexandria

To my parents

Who gave me a lot of support

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Contents

INTRODUCTION

RENAL TRANSPLANTATION

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End stage renal disease (ERSD) is considered the point of irreversible renal functional deterioration beyond which life can no longer be sustained without renal replacement therapy in the form of haemodialysis, peritoneal dialysis and transplantation.(1)

Improvements in immunosuppression along with better treatment and prophylaxis for infections complication have made renal transplantation the treatment of choice for most ESRD patients, all patients with ESRD are considered candidates for renal transplantation unless they have systemic malignancy, chronic infections, severe cardiovascular diseases or neuropsychiatry disorders. Renal transplantation can be performed before patients requiring dialysis. Ultimately the patients is responsible for choosing between dialysis and transplantation as options for renal replacement therapy.(2)

The advantages of renal transplantation are clearly established as being prolonging the survival for recipient, improve quality of their life, so can enjoy unrestricted activities and can return to their previous full term employment. There are many successful renal transplant recipients who are followed for up to twenty years as a direct consequence of both improved understanding of tissue typing and immunosuppression.(3)

Efforts were mainly directed towards reducing fatality and morbidity after renal transplantation, patients mortality tend to be highest during the first year after operation, infection was the cause of death of 50% of patients. The second major cause of death during the first year post transplant is cardiovascular complications especially in elderly and diabetic patients. Also inspite of increasing success of renal transplantation, rejection of the transplanted kidney by the recipient still remains the major problem to be overcome, so one of the most important steps in the evaluation process for kidney donation is tissue typing.[4]

Transplantation immunobiology

Major histocompatibility complexes:

The human major histocompatibility complexes (MHC) proteins were first discovered in the 1950s, when it was recognized that many people, specially those who had received multiple blood transfusion or had been pregnant several times, had antibodies in their serum that reacted against a new class of surface glycoproteins on leukocytes from other members of the population. The membrane proteins recognized by these antibodies were termed human leukocyte antigens (HLA), a term that is still used as a synonym for the human MHC proteins. It was soon realized that these same HLA molecules could also be targets of cellular immunity, HLA proteins are

usually the main target of the cellular immune reactions that cause rejection of solid tissues transplanted between unrelated individuals.[5]

Transplantation antigens are classified according to their relative potencies in eliciting rejection as either major or minor. The incompatibility of MHC antigens between a donor and recipient of an allograft leads to graft rejection.[6]

MHC is a complex of genes found in all vertebrates and in humans has been located on the short arm of chromosome 6. The MHC genes in humans encode polymorphic cell surface molecules, HLAs.[7] (Figure 1)

The polymorphism of HLAs involve specific hypervariable regions of the molecule and constitute both to self recognition and to antigen binding. HLA gene products are inherited in a mandelian codominent fashion which means, that all six class I alleles are expressed together on the surface of every nucleated cell.[7]

There are three separate genes, designated HLA-A,-B, and -C, that each code for classical MHC class I. Similarly there are three classical MHC class II gene loci, known as HLA-DP,-DQ and -DR, each of which includes genes for one α and at least one β polypeptide. A person normally inherits two copies of each gene locus, one from each parent, and so carries a total of six class I and six class II loci.[8]

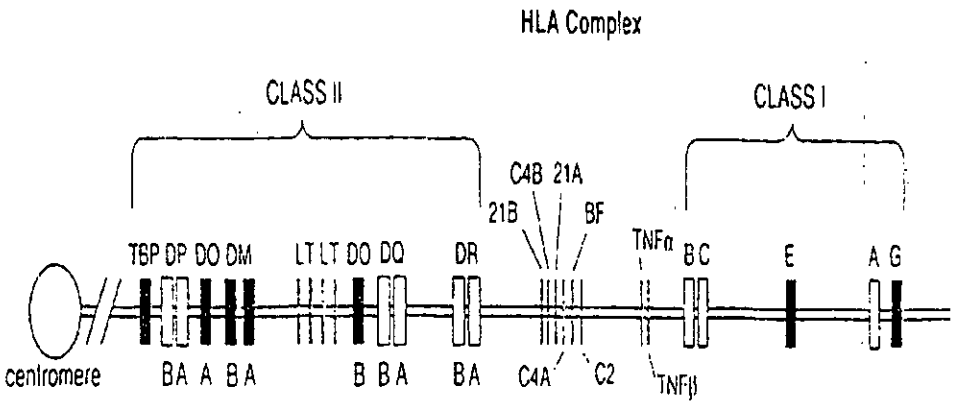

Figure 1: Organization of the HLA gene complex on the short arm of human chromosome 6.[7]