Hla Typing Epitopes

The human leukocyte antigen (HLA) or tissue types are the products of a rapidly developing field of knowledge within the last 20 years. In the early stages of the research many investigators suspected the existence of a complex series of transplantation antigens, but it was widely believed that these antigens would not be well-defined even in this century. Yet in the last two decades as many as 124 different HLA antigens determined by at least 7 very closely linked genes located on the short arm of chromosome 6 have been identified and subsequently agreed upon by an international nomenclature committee. Extensive international collaboration fueled by the potential clinical application of these antigens to clinical transplantation has advanced the field rapidly. There were nine international histocompatibility workshops held during this period. Although identification of HLA antigens was of primary clinical importance in transplantation and of great basic interest in human genetics and anthropology, a rather unexpected bonus has been the determination that HLA antigens are associated with disease susceptibility to a greater extent than any other known genetic marker in man. In the past, many genetic polymorphisms have been suspected to be associated with diseases. The most extensively studied markers are blood groups, enzymes, and serum proteins. A comprehensive account of published studies, totalling approximately 1,000, of these markers is available in a book by Mourant et al.

A detailed, contributed reference offering broad coverage of renal transplantation in children. Diagnosis, the patient's medical management, operative methods, surgical and medical complications, donor selection, immunosuppression, late effects on growth and development and psychosocial factors are among the topics discussed. Features a chapter on how to set up and manage a pediatric renal transplant program.

With this book we want to address young graduate students, clinicians involved in transplantation, and technicians in transplantation immunology laboratories. The volume should give a comprehensive but basic, up to date introduction to the structure, function, and clinical importance of the HLA system. We believe that there is a need for such a survey, and think that the present level of our knowledge is an optimal occasion for publication. A significant number of questions have now been resolved, and our knowledge has reached a level of sophistication that provides the basis for additional questions and answers. Although the emphasis of this book is on the role of HLA antigens in clinical transplantation, their involvement in other clinical contexts is also discussed. The main focus is on the human MHC antigenic system, but MHC systems in other species are described as they contribute to our understanding of the structural and functional characteristics of HLA antigens. Some important issues related to laboratory techniques are also covered. The contributors have a close affiliation to the field of transplantation immunology. A majority have even been playing important roles in unraveling the HLA system and its functions. We believe this has contributed significantly to the quality and clinical and practical relevance of the book. As editors, we drew up the principal guidelines and took care that the chapters can be read as separate entities, although this invariably results in some overlapping.
The first real major breakthrough that laid the basis of HLA antibody detection in the field of solid organ transplantation, came with the introduction of the complement dependent cytotoxicity (CDC) test in 1964 by Terasaki and McClelland. Since then, methods for antibody detection have evolved remarkably from conventional cell-based assays to the current advanced solid phase systems on the Luminex platform, with increasing degree of sensitivity and specificity. The latter have been indispensable for more accurate identification of donor specific HLA antibodies in broadly reactive allo antisera, and to guide donor selection and kidney paired exchange programs through virtual crossmatching, in addition to serving as excellent tools for initiating pre-transplant desensitization and post- transplant antibody monitoring. Consensus is evolving on the optimal routine employment of these methods in donor selection strategies along with an understanding of the clinical relevance of antibodies detected by each of them. The immunoassays based on the Luminex platform and flow cytometric beads are however unable to discriminate complement fixing from non-complement fixing HLA antibodies. This is important because the former are considered clinically more pertinent in the peri-transplant period. The C1q assay which is a modification of the solid phase assay based on Luminex single antigen beads, which can be used effectively to monitor high dose IVIG desensitization is essentially a surrogate complement fixing assay, retaining the exquisite sensitivity and specificity of the Luminex platform. Currently, information obtained from these assays is preliminary and much needs to be done to standardize technologies and set a consensus ‘MFI cut off’ for antibody positivity. Besides the overriding influence of anti-HLA antibodies on overall solid organ graft survival, immune response to non-HLA antigens has become a topic of substantial interest in recent years. An ever expanding list of non-HLA antigens has been implicated in graft rejection for various organs, of which the most noted are the Major Histocompatibility Complex class I chain-related molecule A (MICA), Vimentin, Myosin, Angiotensin II type 1 receptor (AT1R), Tubulin and Collagen. MICA is one of the most polymorphic and extensively studied non-HLA antigenic targets especially in renal transplantation. Although there are clear indications of MICA antibodies being associated with adverse graft outcome, to date a definitive consensus on this relationship has not been agreed. Because MICA molecules are not expressed constitutively on immunocompetent cells such as T and B lymphocytes, it is of utmost importance to address the impact of MICA donor specific antibodies (DSA) as compared to those that are non- donor specific (NDSA) on graft outcome. The soluble isoform of MICA molecule (sMICA) that is derived from the proteolytic shedding of membrane bound molecules has the potential to engage the NK-cell activating receptor NKG2D and down-regulate its expression. Consequent to the interaction of NKG2D by sMICA, the receptor ligand complex is endocytosed and degraded and thus suppresses NKG2D mediated lysis of the target by NK cells. Thus interaction between NKG2D and sMICA leads to expansion of immunosuppressive/anergic T cells thereby resulting in suppression of NKG2D mediated host innate immunity. These concept support the possible involvement of an immunosuppressive role for sMICA during allotransplantation as shown recently for heart transplantation. This research topic focusses on the clinical utility of investigating the complete antibody repertoire in solid organ transplantation.
Leukocyte culture conferences have a long pedigree. This volume records some of the scientific highlights of the 16th such annual conference, and is a witness to the continuing evolution and popularity of leukocyte culture and of immunology. There is strong evidence of the widening horizons of immunology, both technically, with the obviously major impact of molecular biology into our understanding of cellular processes, and also conceptually. Traditionally, the 'proceedings' of these conferences have been published. But have the books produced really recorded the major part of the conference, the informal, friendly, but intense and some times heated exchanges that take place between workers in tackling very similar problems and systems and which are at the heart of every successful conference? Unfortunately this essence cannot be incorporated by soliciting manuscripts. For this reason, we have changed the format of publication, retaining published versions of the symposium papers, but requesting the workshop chairmen to produce a summary of the major new observations and areas of controversy highlighted in their sessions, as a vehicle for defining current areas of interest and debate. Not an easy task, as the workshop topics were culled from the abstracts submitted by the participants, rather than being on predefined topics. The unseasonal warmth in Cambridge was reflected in the atmosphere of the conference, the organization of which benefited from the administrative skills of Jean Bacon, Philippa Wells, Mr. Peter Irving, and Mrs. After decades of research in clinical transplantation, new techniques have been developed that permit a further understanding of the immune mechanisms underlying immune recognition of allografts and a more accurate and thorough evaluation of compatibility between donors and recipients. The second edition of Transplantation Immunology: Methods and Protocols expands upon the previous edition with current, detailed methods in transplantation immunology. The new methods chapters cover four major areas that are being applied in compatibility evaluations and ongoing transplantation immunology research. Seven overview chapters provide reviews of the molecular basis for alloreactivity, current understanding of humoral and cellular mechanisms, as well as new developments in thoracic organ transplantation, composite tissue transplantation and in the transplantation of sensitized patients. Written in the highly successful Methods in Molecular BiologyTM series format, chapters include introductions to their respective topics, lists of the necessary materials and reagents, step-by-step, readily reproducible laboratory protocols, and key tips on troubleshooting and avoiding known pitfalls. Authoritative and practical, Transplantation Immunology: Methods and Protocol, Second Edition is devoted to transplantation immunology, both in the practice of compatibility testing and in transplantation research. This volume documents our growing understanding of the human major histocompatibility complex. The application of this information is ever more important as the limits of transplantation continue to be reduced, including the recent success of bone marrow transplantation between unrelated but closely matched individuals. In addition, the need to transfuse platelets in the face of immunologic barriers continues to challenge transfusion services. Thus, the serologic information summarized in this volume is essential for optimal patient care. At the same time, recombinant DNA technology has led to a revolution in our understanding of many aspects of basic biology. Among the advances has been the initial characterization of the structure of some HLA loci. While this will ultimately improve clinical services, constant reference to serologic data is essential so that the powerful new techniques can be applied in the most effective ways. The timing of the First Red Cross International Histocompatibility Workshop is fortunate as it brings together experts from around the world to address the state of the art. We are all grateful to Dr. John Lee and his colleagues for organizing the workshop, and for bringing together
in this volume the material to be presented in Beijing during October 17-23, 1990. Leon W. Hoyer, M.D. This comprehensive and definitive work succeeds and expands on the highly successful HLA and Disease published in 1994. This new edition has been updated, redesigned and reorganised into three sections making it an invaluable reference. The introductory section summarises current knowledge on the structure, function, genetics and evolution of the HLA system. It clarifies its complex and ever changing nomenclature and discusses the mechanisms underlying disease associations with HLA alleles. The second section deals with the importance of HLA in the context of different clinical specialities. Individual chapters describe the association between HLA polymorphism and each disease. The final section features chapters on current laboratory practice in histocompatibility and tissue typing. HLA in Health and Disease is essential reading for basic and clinical researchers working in immunology and immunogenetics, transplantation medicine and autoimmunity. It will also be of interest to anyone in the fields of rheumatology, diabetology, nephrology, allergy, dermatology, neurology, endocrinology, cancer biology, respiratory medicine, haematology, molecular biology and biochemistry. Key Features Structure, function and genetics of HLA HLA nomenclature Evolution of HLA polymorphisms HLA associations in arthritis and rheumatology, renal disease, neurology, diabetes and endocrinology, gastroenterology, respiratory disease, ophthalmology, infections, dermatology and psychiatry HLA and organ transplantation Serological and PCR-based methods in HLA typing Cellular techniques in testing histocompatibility Edited and written by an international panel of experts in the field Immunobiology of HLA History of HLA MHC Ligands and Peptide Motifs Recent Trends in Immunology Ten Recollections In contrast to existing books on immunoinformatics, this volume presents a cross-section of immunoinformatics research. The contributions highlight the interdisciplinary nature of the field and how collaborative efforts among bioinformaticians and bench scientists result in innovative strategies for understanding the immune system. Immunoinformatics is ideal for scientists and students in immunology, bioinformatics, microbiology, and many other disciplines. This book is centered on a comprehensive list of MHC peptide motifs and ligands as known to date, together with selected T cell epitopes, arranged in an easy-to-read fashion. This information is put into context by chapters on MHC gene organization, MHC structure, T cell epitope prediction, antigen processing and T cell responses. In addition, the book provides a great deal of complementary information: amino acid sequences of MHC class I alpha1 and alpha2 domains and of class II alpha1 and beta1 domains, the established or predicted composition and specificity of MHC pockets, notes on MHC nomenclature including old assignments and reference to useful internet addresses. A handy reference manual that should be helpful for all those dealing with MHC-associated peptides. This comprehensive encyclopedic reference provides rapid access to focused information on topics of cancer research for clinicians, research scientists and advanced students. Given the overwhelming success of the first edition, which appeared in 2001, and fast development in the different fields of cancer research, it has been decided to publish a second fully
revised and expanded edition. With an A-Z format of over 7,000 entries, more than 1,000 contributing authors provide a complete reference to cancer. The merging of different basic and clinical scientific disciplines towards the common goal of fighting cancer makes such a comprehensive reference source all the more timely.

Antibody Repertoire and Graft Outcome Following Solid Organ Transplantation
Frontiers Media SA

Epitope Discovery and Synthetic Vaccine Design
HLA and Disease, An Issue of the Clinics in Laboratory Medicine
The HLA System in Clinical Transplantation
Advances in Ebola Control
The HLA System

This volume focuses on the evidence for or against molecular mimicry as a cause of autoimmunity. Contributions from recognized experts present their original findings, and the final chapter reviews the overall perspective of molecular mimicry, how to use its principles in clinical investigation and list the conceptual traits by which autoimmune disease can occur.

The HLA FactsBook presents up-to-date and comprehensive information on the HLA genes in a manner that is accessible to both beginner and expert alike. The focus of the book is on the polymorphic HLA genes (HLA-A, B, C, DP, DQ, and DR) that are typed for in clinical HLA laboratories. Each gene has a dedicated section in which individual entries describe the structure, functions, and population distribution of groups of related allotypes. Fourteen introductory chapters provide a beginner's guide to the basic structure, function, and genetics of the HLA genes, as well as to the nomenclature and methods used for HLA typing. This book will be an invaluable reference for researchers studying the human immune response, for clinicians and laboratory personnel involved in clinical and forensic HLA typing, and for human geneticists, population biologists, and evolutionary biologists interested in HLA genes as markers of human diversity. Introductory chapters provide good general overview of HLA field for novice immunologists and geneticists Up-to-date, complete listing of HLA alleles Invaluable reference resource for immunologists, geneticists, and cell biologists Combines both structural and functional information, which has never been compiled in a single reference book previously Serological specificity of allotypes Identity of material sequenced including ethnic origin Database accession numbers Population distribution Peptide binding specificities T cell epitopes Amino acid sequences of allotypes Key references

This volume explores the rapidly evolving field of HLA typing and its use in both the laboratory setting and in silico methods. The chapters in this book discuss high-throughput methods for HLA typing; wet lab protocols; microarray data and its uses; in silico tools for the identification of HLA alleles from DNA and RNA next-generation-sequencing data, as well as HLA haplotype frequency estimation. Written in the highly successful Methods in Molecular Biology series format, chapters include introductions to their respective topics, lists of the necessary materials and reagents, step-by-step, readily reproducible laboratory protocols, and tips on troubleshooting and avoiding known pitfalls. Cutting-edge and practical, HLA Typing: Methods and Protocols is a valuable resource for any researcher interested in learning more about this developing field. Technical innovations in the laboratory over the past ten years have greatly improved our understanding of the immunological mechanisms of transplanted organ rejection. In Transplantation Immunology: Methods and Protocols, leading experts in solid organ transplantation review the current status of the field and describe cutting-edge techniques for detecting the immune response to the allografted organ. The authors present the latest techniques for HLA typing, detecting HLA antibodies, and monitoring T-cell response, and examine more specialized methods of utilizing proteomics, laser dissection microscopy, and real-
time polymerase chain reaction. The areas of tolerance induction and reprogramming of the immune system are also covered, along with a discussion of up-to-date methods of organ preservation, of today's optimal immunosuppressive drug regimens, as well as the difficulty of mimicking chronic rejection in experimental models. Introductory chapters provide a theoretical update on current practices in renal, liver, islet, and lung transplantation and on the pathways of antigen presentation and chronic rejection. State of the art and highly practical, Transplantation Immunology: Methods and Protocols illuminates for clinicians and scientists--both newcomers and experts--the new world of detecting and monitoring patients' immunological responses to solid organ transplantation.

Immune Regulation
Validation of the Method, Improved Epitope Prediction, Peptide-based HLA Typing and Discrimination of Healthy and Malignant Tissue
Pediatric Renal Transplantation
Identification and Characterization of HBV Core CTL Epitopes in Indonesian Samples
Bone Marrow and Stem Cell Transplantation

This year marks the 60th anniversary of HLA discovery by the French Nobel laureate physician Jean Dausset, as well as the 55th anniversary of the identification and naming of the first HLA. Under such circumstances, both basic HLA research and its clinical applications need a new book that comprehensively reflects the latest achievements in the field. Thus, Professor Xi as Editor has contributed to organize international experts in the areas of HLA-related basic research and clinical applications, to unite their knowledge in chapters covering various related topics, and finally to finish the book "HLA and Associated Important Diseases". The book consists of three sections which mainly include basic theoretical and technological developments, several important HLA-associated autoimmune diseases and HLA-associated infectious diseases.

Taken together, these results indicate that selection of HLA matched platelets by epitope matching using ePlatelets represents an effective HLA matching strategy for patients IR to random platelet transfusions.

This book is for statistical practitioners, particularly those who design and analyze studies for survival and event history data. Building on recent developments motivated by counting process and martingale theory, it shows the reader how to extend the Cox model to analyze multiple/correlated event data using marginal and random effects. The focus is on actual data examples, the analysis and interpretation of results, and computation. The book shows how these new methods can be implemented in SAS and S-Plus, including computer code, worked examples, and data sets.

The here presented book covers different areas of clinical and scientific interest, reaching from donor evaluation to newest methods in immunological diagnostics. But also aspects of daily care of transplant recipients can be found in the carefully selected chapters. Everything driven by the aim to improve the care for all of our transplanted patients.

Modeling Survival Data: Extending the Cox Model
Epitope-based Re-matching of Donor-recipient Pairs for Kidney Graft Allocation
Basic Concepts and Importance
In Silico Discovery of Novel Cytotoxic T-lymphocyte Epitopes in the HIV-1 Pol
Region in Response to Antiretroviral Resistance Mutations

HLA Typing

Since the original publication of Allogeneic Stem Cell Transplantation: Clinical Research and Practice, Allogeneic hematopoietic stem cell transplantation (HSC) has undergone several fast-paced changes. In this second edition, the editors have focused on topics relevant to evolving knowledge in the field in order to better guide clinicians in decision-making and management of their patients, as well as help lead laboratory investigators in new directions emanating from clinical observations. Some of the most respected clinicians and scientists in this discipline have responded to the recent advances in the field by providing state-of-the-art discussions addressing these topics in the second edition. The text covers the scope of human genomic variation, the methods of HLA typing and interpretation of high-resolution HLA results. Comprehensive and up-to-date, Allogeneic Stem Cell Transplantation: Clinical Research and Practice, Second Edition offers concise advice on today's best clinical practice and will be of significant benefit to all clinicians and researchers in allogeneic HSC transplantation.

The practical aspects of flow cytometry and sorting are emphasized in this book which introduces the beginner to the technology and provides tips and tricks for the advanced user. The clear structure makes it easy to address specific problems fast. The chapters cover the modern applications of these procedures, with emphasis on immunofluorescence (antibody-fluorochrome conjugation, staining principles and data evaluation); the isolation of specific chromosomes, cells and fragile, large particles by magnetic and fluorescence-activated sorting; cellular biochemistry; and the dynamics of proliferation. The methods have been field-tested in recent EMBO courses on flow cytometry.

M. BENcovA Slovak Foundation Education in Immunogenetics Kopanice 25, 821 04 Bratislava Slovak Republic Short History of Slovakia After the end of the 5th century, the major part of Central Europe was dominated by Slavs (Slovaks). They had already in the 7th century settlements in the vicinity of towns Bratislava, Devin, Nitra to create the Slovak's state formation with the name "The Empire of Sam", territory of which corresponded to that of Slovakia of present. The Empire of Sam was also the first state formation in the
Central Europe (as present states Czech Republic, Poland, Hungary, Slovakia etc.) Very important town of this state was Nitra, with the biggest Castle in the Central Europe with his Duke Pribina. The first Church of the Central Europe was built here in the year 830, and it is now considered to be the "Slovak Bethlehem". In the year 880, Nitra also became the first Office of Bishops. Later, the Slovak Duke Pribina and Moravian Duke Mojmir (Moravia corresponded to eastern part of the present Czech Republic) joined their formations to common state "Greate Moravian Empire". The strongest King of the Great Moravian Empire was Svatopluk (864 A. D.), who spread his empire over Czech Republic, Hungary and part of Poland, Ukraine and eastern Germany of present, which at that time still did not exist as state formations.

The second edition of Bone Marrow and Stem Cell Transplantation expands upon the previous edition with current, detailed methods on HLA, minor-HLA and Killer Immunoglobulin Like Receptor typing. With new chapters on immunophenotyping and functional characterization of stem cells are included. Written in the highly successful Methods in Molecular Biology series format, chapters include introductions to their respective topics, lists of the necessary materials and reagents, step-by-step, readily reproducible laboratory protocols, and tips on troubleshooting and avoiding known pitfalls. Authoritative and practical, Bone Marrow and Stem Cell Transplantation, Second Edition serves as a guide in the application of molecular methods for routine or investigational purposes.

HLA and Associated Important Diseases
Flow Cytometry and Cell Sorting
Advancing Immunopeptidomics
Current Issues and Future Direction in Kidney Transplantation

Hepatitis B virus (HBV) is a non-cytopathic virus that causes liver disease with variable duration and severity. During infection, host immune response is responsible for both liver damage and viral clearance. The adaptive immune response, particularly virus-specific cytotoxic T lymphocyte (CTL) response, has been shown to play a major role in HBV infection immunopathogenesis by destroying the infected hepatocytes or eliminating HBV in a non-cytolytic manner. From virus-host interaction perspective, HBV core antigen (HBcAg) has been of interest because it is a major immunological target of CTL. Many human leucocyte antigen (HLA)-restricted HBcAg T cell epitopes have been reported which might be different due to the diverse distribution ethnic-specific HLA in distinct geographical regions. Therefore, it is important to identify and characterize HBcAg CTL epitopes in area with high HBV endemic and high population diversity like Indonesia. To support HBcAg as a promising protein to develop CTL epitope-based vaccine,
HBcAg sequences of samples from individuals in Indonesia were analyzed. It was found that the sequences were conserved, and amino acid substitutions observed did not reflect the influence of human leucocyte antigen (HLA) types on the HBcAg variability. To develop such a vaccine, the first thing to do is to determine the peptide(s) that must be immunogenic and can interact with HLA class I proteins of Indonesian populations. Using immunoinformatic approaches, 20 HBcAg CTL epitopes (14 nonamers and 6 decamers) against HLA alleles in Javanese, Sundanese-Javanese, and Ternatean populations were identified. These 20 CTL epitopes were also characterized for sequence variation and conservation in 125 HBcAg of Indonesian isolates. Variations of HBcAg CTL epitope were detected, but one variant was found to be predominant in each epitope. By immunoinformatic analysis, different binding affinity was observed for each variant. The difference was found to depend on the location and type of amino acid in related epitope that affect its interaction with HLA binding grooves. The present study describes the use of immunoinformatic approaches as a pilot study to identify HBcAg CTL epitopes of Indonesian isolates and analyze their conservation and variability. Of 20 CTL epitopes, HBcAg 18-27 was found the best CTL epitope for the Indonesian populations represented by the Javanese, Sundanese-Javanese, and Ternatean. Among the discovered epitope variants, residue FLPSDFFPSI was identified as the best candidate to develop peptide-based vaccine due to its predominance among all isolates studied. This study will be beneficial for developing an approach for successful viral control in hepatitis B patients.

This issue of Clinics in Laboratory Medicine, edited by Drs. Julio Delgado and Eszter Lazar-Molnar, will focus on HLA and Disease. Topics include, but are not limited to, The potential impact of NGS in HLA and disease association studies, HLA typing by NGS, HLA Antibody Testing: Evolution and Challenges, Diversity of killer cell immunoglobulin-like receptors and disease, Technical Aspects of Crossmatching in Transplantation, HLA Markers in Celiac Disease, HLA Associations in Drug Hypersensitivity Reactions, HLA in BMT, Post-transplant monitoring, HLA epitope matching in transplantation, and Molecular Testing in Post-Transplant Monitoring.

The Acquired Immunodeciency Syndrome pandemic continues to have a large social impact. Many advances in the treatment of infection by the causative agent, Human Immunodeciency Virus, have been made in the last three decades. However, this treatment often means a life-long rigorous adherence to treatment and acquisition of resistance mutations to antiretrovirals. Thus far, the efficacy of promising vaccines has been disappointing. In the last decade, interest has grown concerning the interaction between mutations conferring resistance to antiretrovirals and the effect this has on epitopes recognized by cytotoxic-T-lymphocytes (CTL). Investigating this is a difficult task, owing to both the extreme polymorphism of HIV and the polymorphism of the Human Leukocyte Antigen (HLA) molecules that present peptides to the CTLs. A large amount of HLA-associated CTL escape mutations have been discovered. Together with this, computational approaches in CTL epitope discovery is becoming increasingly accurate. Here, a method of imputing HLA type from patients together with predicting the influence of antiretroviral mutations was used to discover potential epitopes for the HLA B*15 and B*48 types in the HIV-1 Subtype B pol region. This invaluable book provides comprehensive coverage of contemporary serological, cellular and molecular methodologies in histocompatibility testing, and their application to human organ transplantation and transfusion. The contributors are internationally respected authorities in histocompatibility and immunogenetics, and are closely involved in the development or application of state-of-the-art technologies. The first three sections of the book are primarily intended for use as a bench manual for histocompatibility testers, immunologists and immunogeneticists; the fourth and fifth sections, on selection of donors and statistical methods, will further assist medical practitioners involved in clinical transplantation and its outcome. The final section of the book reviews the genetics and clinical relevance of minor histocompatibility antigens. Contents: Foreword:HLA Polymorphism: Origin and Maintenance (W F Bodmer)Introduction:Immune Recognition and the MHC (P Travers)Antibody-Based Histocompatibility TestingHLA Typing by Allelotypes and Monoclonal Antibodies (G M Th Schreuder)Screening for HLA-Specific Antibodies (C Brown & C Navarrete)Detection of Soluble HLA (V Rebmann & H Grosse-Wilde)Crossmatching by Lymphocyte toxicity and Flow Cytometry (S Martin & A Hamer)DNA-Based Histocompatibility TestingPCR-SSP Typing (M Bunce)PCR-SSOP Typing (D Middleton)Sequencing-
When considering the matching of donor and recipient pairs for kidney transplantation, there are many aspects that must be compared and evaluated in order to ensure the best outcomes for recipients. Historically, a focus has been placed on evaluating the number of mismatches in various loci of Human Leukocyte Antigens (HLAs) in addition to other clinical factors including blood type, history of disease, etc. While HLA is still a standard technique for determining the histocompatibility of donor-recipient pairs, recent research has shown that other methods such as immunogenicity scores and eplet load may provide a more nuanced approach to donor-recipient matching, resulting in the ability to increase both quantity and quality of kidney transplants that occur. Based on evidence that eplet-based matching may provide improved outcomes for kidney transplant recipients, this thesis develops computational tools, namely a small Python-based library, to aid in the evaluation of this matching methodology and explores data in order to demonstrate computationally the potential impacts of eplet load-based matching when considering race. A secondary evaluation is also made to see how introducing an additional HLA (HLA-DQ) potentially affects re-matching success. Results demonstrate that matching on eplet load yielded an average 8x increase in matches than when using HLA mismatches.
Umbilical cord blood (UCB) and, more recently, umbilical cord tissue (UCT) have been stored cryopreserved in private and public cord blood and tissue banks worldwide, since the umbilical cord blood was used for the first time in a child with Fanconi anemia with his HLA-identical sibling, following strict guidelines that imply high-quality standards and total rastreability of these units. The hematopoietic stem cells (HSCs) are clinically used in hematopoietic treatments for blood disorders and hemato-oncological diseases. Also, the mesenchymal stem cells (MSCs) isolated from the UCT and UCB, nowadays, can be used as coadjuvants of hematopoietic transplants. In the near future, these stem cells will have a crucial role in regenerative medicine. For this reason, these cells have been tested in several clinical trials and compassionate treatments in children and adults, concerning a wide range of pathologies and diseases, for instance, for the treatment of cerebral paralysis. Considering the worldwide availability of UCB and UCT units and the absence of ethical concerns will probably become the best sources for cell-based therapies for hematological and nonhematological pathologies. The UCB will also have a crucial role in neonatology-predictive analysis in the near future.