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SERVICE PROVISION

INTRODUCTION

Here at Anthony Nolan, we save the lives of people with blood cancer. We use our register to match incredible individuals willing to donate their bone marrow to people in desperate need of transplants. We conduct pioneering research into the treatment of bone marrow disorders and look for new ways to improve the effectiveness of bone marrow transplants.

Right now we have more than 490,000 potential haematopoietic stem cell (HSC) donors on our register and to date we have facilitated more than 10,000 transplants. Our aim is to "provide a lifesaving transplant for every person who needs one. We do this by maintaining our register, through focused donor recruitment, retention and tracing strategies.

The Anthony Nolan Laboratory provides Histocompatibility and Immunogenetics (H & I) services to donors and patients awaiting HSC transplants and to the liver and renal transplant patients of the Royal Free Hospital. In addition the laboratories provide Human Leukocyte Antigen (HLA) related disease association and drug-resistance testing.

This prospectus is aimed at the following individuals and organisations to ensure that all those affected by the services provided by Anthony Nolan Histocompatibility Laboratories are informed of the processes undertaken:

• Transplant centres and H &I staff in the UK and overseas
• General practitioners
• Patients in need of a HSC transplant and their families in the UK and overseas
• Potential HSC donors
• Government agencies
• The wider national and international scientific and medical community
• Anthony Nolan supporters and fundraisers
• International registries
• Hospital haematology units
Our organisation is made up of several departments, all working together to ensure we save as many lives as we can.

This brochure outlines the services specifically offered by the Anthony Nolan Histocompatibility Laboratories. For a comprehensive overview of the services we provide, take a look at the Anthony Nolan Operations Service User Guide. (http://www.anthonynolan.org/Healthcare-professionals/Services/Operations-user-guide.aspx)

Our other departments also have an important role to play in achieving our aim, such as scientific research, information technology and fundraising. For further details of these departments please visit http://www.anthonynolan.org.

We act as the UK’s ‘hub’ for volunteer unrelated HSC transplantation.

As such, Anthony Nolan co-ordinates all aspects of extending a donor search internationally, from foreign donor and cord blood sample requests through to donor work-up for donation and import of haematopoietic stem cell products.
Identification of a related donor for a patient

When a patient is identified as potentially requiring a HSC transplant, the first step is to perform HLA typing on the patient and any available and suitable relations, usually siblings.

HLA typing of patients is performed by our Histocompatibility Laboratories. Request forms are available by contacting laboratories@anthony Nolan.org or are downloadable from www.anthonynolan.org for those individuals with access. Patients are screened for certain transmittable viruses and are ABO/RhD blood group typed (see Section 5.2).

HLA typing of potential related donors is undertaken to identify a suitable match.

CMV screening and blood grouping is also performed. Where sibling HLA typing is undertaken there is a 25% chance that a suitable match will be identified for a patient in need of a haematopoietic stem cell transplant. Whenever possible, HLA typing of parents should be performed to confirm the patient’s type and to accurately determine HLA haplotypes within a family.

For final selection of a related donor, HLA typing of both patient and selected donor must be confirmed on a second sample such that results are verified prior to transplant.

For those patients where a related matched donor is not identified, the search can be extended to identifying a matched unrelated donor or a cord unit from the register. In some circumstances an extended family search may be performed (see box 1, Page 7) or a HLA haplotype mismatched related donor may be considered.

If a patient has more than one haploidentical family member to choose from, several 9/10 unrelated donors with different mismatching HLA antigens, or a choice of several potential cord donors (see below) with different mismatching HLA antigens to the patient, studies have indicated it is better to avoid choosing a donor for whom the patient has HLA antibodies directed against the mismatched donor antigen. Such patient HLA antibodies are called Donor Specific Antibodies (DSA) and if present can increase the chance of graft rejection.

HLA antibody screening and identification is a service we can provide at Anthony Nolan. We would recommend the use of this technique to help assist in donor
selection in the situations outlined above.

Advice on matching donors and patients can be provided by us. However, the final decision on donor suitability is always the responsibility of the transplant centre.

**Box 1**

*If requested, extended family searches may be performed if a sibling match or unrelated donor match is not available.*

Relatives, such as grandparents, aunts, uncles or cousins, may share one of the patient’s haplotypes and it may be possible that the patient’s second haplotype (or a closely matched second haplotype) is introduced into the family via spouses.

Even a child of the patient could be a match. Extended family searches are advisable if the patient possesses at least one haplotype that is considered common within the general population. The extended family search should focus on analysis of the side of the family from which the least common haplotype is inherited, in the hope that the frequent haplotype has been introduced through marriage. Extended family searches may also be undertaken if the patient is from an ethnicity not widely represented on donor registers.

*In the diagram below, the patient has inherited a rare haplotype from his father and a common haplotype from his mother.*

His cousin also shares the same phenotype, with the same rare haplotype inherited from the cousin’s father and the second haplotype inherited from the cousin’s mother, who is unrelated to the patient.
4.1 Verification typing of potential matched donors / cord blood units identified

Once potential matched unrelated donors are identified, their HLA type must be verified. Blood samples are requested from the unrelated donors (on our register or any other register where a potential matched donor has been identified). It is necessary to request a fresh sample from prospective donors. It is recommended that virology screening is performed on a recent blood sample. HLA typing of matched unrelated donors can be performed by the transplant centre’s designated laboratory or by our laboratories. HLA typing at our Histocompatibility Laboratories is performed by the same procedures as described for the patient, including high resolution typing. Results will not be issued until all tests including virology and blood group testing are complete. The results of donor HLA typing performed outside of Anthony Nolan must be sent to our Operations Division. If the donor is no longer required, the Operations Department should be informed such that the donor can be released and made available for other patient searches. Where necessary, donors can be placed on hold (maximum 90 days) to allow the Transplant Centre to resolve issues with the conditioning of the patient. This information is crucial not only for our donors but also donors provided by international registries.

At this time it is necessary to perform verification typing on a second sample from the patient, if this has not been previously performed. This step eliminates any remote possibility of sample error at the time of initial bleed and typing. Please bear in mind European Federation for Immunogenetics (EFI) standards which requires these verification samples to be “independently” collected.

EFI guidelines also dictate that before the commencement of any conditioning regimen of any cord blood recipient, a verification typing of at least HLA-A, -B, and -DRB1 at a minimum level of low resolution should be performed upon reception of the shipped unit (in addition to any verification typing already performed). Typing must be performed on a segment of the tubing integrally attached to the unit, if available. Otherwise a satellite vial shipped with the unit may be used. If no segment is available, this step can be
performed after transplantation and must be initiated as soon as possible after thawing the unit. In such cases whatever material left over from the infusion must be sent by the receiving Transplant Centre to our Histocompatibility Laboratory for verification typing as outlined in section 6.1 If the Transplant Centre routinely utilises an alternative H&I laboratory for clinical service testing, the cord segment or vial should be sent to their usual service provider as per their instructions.

4.2 Post-transplant Chimerism Monitoring

Post-transplant chimerism monitoring can be undertaken on request. Please contact laboratories for further details: laboratories@anthonynolan.org

4.3 Target turnaround times

We aim to process and report at least 75% of patients, potential related and unrelated donor samples within seven working days.

4.4 Solid organ transplantation

The Histocompatibility Laboratories, Solid Organ team, provides a service to support the requirements of the renal and liver transplant units of the Royal Free Hospital, London. This service is funded by the Royal Free London NHS Foundation Trust.

4.5.1 Renal transplantation

For kidney transplantation, potential recipients are HLA typed by serological (HLA-A, -B) and DNA based methods: HLA-A, -B, -C, -DRB1,-DRB3,-DRB4,-DRB5,-DQA1, -DQB1. HLA-DPA1 and HLA-DPB1 testing is performed where appropriate. Two independent samples are tested for each patient. Patients are also screened for HLA alloantibodies and if present, the specificity of such antibodies is defined. Patients are screened at three monthly intervals in accordance with British Transplantation Society standards (www.bts.org.uk). Confirmatory blood group typing is also performed on all patients. Family members may also be HLA typed to resolve patient’s HLA haplotypes and to aid definition of antibodies arising from sensitisation through pregnancy.

The cadaveric transplant waiting list is maintained by Organ Donation Transplantation (ODT), part of National Health Service Blood and Transplant service, Bristol. A 24-hour, seven days a week, on-call service is available to provide tissue-typing and cross-matching facilities on an on-call basis. The North Thames transplant coordinators inform laboratory staff of potential cadaver organ donors in 'local' hospitals and arrange for EDTA blood to be collected and sent to the laboratory for HLA typing. All “local” cadaver donors are HLA typed by serology (HLA-A, -B, -DR, -DQ) and by DNA methods (HLA-A, -B, -C, -DRB1,-DRB3,-DRB4,-DRB5, -DQB1). HLA-DP testing is performed when appropriate. ODT is notified of donor HLA type by facsimile. Non-local donors also have their HLA type confirmed by serology during on-call hours and subsequently by
DNA methods. Crossmatching between donor and potential recipient is performed using both Complement Dependent Cytotoxicity (CDC) and Flow Cytometry methods. This enables detection of the presence of donor specific antibodies in the patient serum, which if present are a contraindication for transplantation. Results are reported to on duty physicians and surgeons.

Where a living related or unrelated donor transplant is being considered, all potential donors are blood group typed to determine compatibility. HLA typing (HLA-A, -B, -C, -DRB1/3/4/5 and -DQB1) is performed to determine compatibility. Crossmatching between patient and potential donor is performed using both CDC and Flow Cytometry methods at the initial time of donor selection and again within 7-14 days of the proposed transplant. All results are communicated in writing to the transplant nurse and clinicians. Serum samples from all recipients of a transplant are received and screened at intervals in accordance to British Transplant Society guidelines.

4.5.2 Liver transplantation

All potential liver recipients are HLA typed by DNA (HLA-A, -B, -C, DRB1/3/4/5, -DQB1) methods. HLA types of cadaver donors are obtained from ODT. Retrospective crossmatching between liver transplant recipients and donors is performed by CDC. All results are communicated in writing to the liver transplant coordinators.

4.5.3 Islet cell transplantation

Potential recipients are HLA typed and HLA antibody screened in the same way as kidney recipients, and registered with ODT. Prior to transplantation, a prospective crossmatch is performed by CDC and flow cytometry which must be negative for a transplant to take place. Results are reported to physicians and surgeons on duty.

<table>
<thead>
<tr>
<th>Service</th>
<th>TAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>New patient on National waiting list</td>
<td>10 days</td>
</tr>
<tr>
<td>Cadaver renal crossmatch</td>
<td>7 hours</td>
</tr>
<tr>
<td>Cadaver liver crossmatch (CDC only)</td>
<td>4 hours</td>
</tr>
<tr>
<td>Live renal donor crossmatch (CDC and Flow Cytometry) + HLA and Blood group</td>
<td>5 days</td>
</tr>
<tr>
<td>Routine HLA antibody screening (by Luminex)</td>
<td>10 days</td>
</tr>
<tr>
<td>Routine HLA antibody screening (by CDC)</td>
<td>90 days</td>
</tr>
</tbody>
</table>
4.6 Disease Associations

HLA typing by DNA methodology will be undertaken to provide support in the diagnosis of the following associated diseases:

<table>
<thead>
<tr>
<th>Disease</th>
<th>Associated HLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankylosing Spondylitis</td>
<td>HLA-B*27</td>
</tr>
<tr>
<td>Narcolepsy</td>
<td>HLA-DRB1<em>15 and -DQB1</em>06</td>
</tr>
<tr>
<td>Behçet’s Disease</td>
<td>HLA-B*51</td>
</tr>
<tr>
<td>Coeliac Disease</td>
<td>HLA-DQ2 and – DQ8</td>
</tr>
<tr>
<td>Abacavir Hypersensitivity</td>
<td>HLA-B*57:01</td>
</tr>
</tbody>
</table>

For more details on disease association tests and costs incurred please contact the laboratory: laboratories@anthonynolan.org

4.7 Haemochromatosis mutation detection

Haemochromatosis is an autosomal recessive disorder which causes an increase in iron absorption leading to iron overload. Two mutations within the HFE gene (found telomeric to the HLA genes on chromosome 6) have been found to be commonly associated with the disorder. These mutations which alter amino-acid 63 (histidine to aspartate) and amino-acid 282 (cysteine to tyrosine) are detected by the PCR-SSP technique. Two additional mutations are also tested: one is a mutation that alters amino acid 65 (Serine to Cysteine) and the other is a splice site mutation (1VS3+1G/T). Please contact the laboratory for a request form. laboratories@anthonynolan.org

4.8 Contract HLA typing

The Histocompatibility Laboratories are able to undertake low and high throughput contract typing when related to the improvement of medical sciences, disease association studies or pharmacogenomic interactions. For more details contact the laboratory: laboratories@anthonynolan.org
5.1 HLA typing

5.1.1 Introduction

HLA typing is performed to define compatibility between donor and patient. An individual’s HLA type is determined by a group of genes which produce proteins expressed on virtually all tissues in the human body. These genes are extremely variable (or polymorphic), making it unlikely that any two random individuals would have an identical HLA type. There are different laboratory methods which are utilised to determine HLA type, and these methods can be divided into two groups. The first is based on the serological recognition of the HLA protein at the cell surface. This test utilises many different antibodies with specificity against different HLA molecules to determine HLA type. The second group of methods work at the DNA level directly, and attempt to identify the genetic make-up of the HLA genes. The HLA system has many different polymorphisms in the population. There are currently over 10000 different HLA alleles (or variants) (http://hla.alleles.org), therefore the typing methods and interpretation of results can appear complex. Although a combination of typing tests is generally performed on each sample, it is not always possible to define the type to a single allele, and frequently results will appear as ‘allele strings’. For example in certain allele combinations for heterozygous loci (majority of individuals are heterozygous at HLA loci) we may not be able to differentiate between the common HLA DRB1*04:01 and the rare HLA DRB1*04:26, and would therefore report the allele string HLADRB1*04:01/26. A full list of HLA alleles currently defined by the WHO Nomenclature Committee for Factors of the HLA System can be found at: http://www.ebi.ac.uk/imgt/hla/

5.1.2 Serological typing

HLA typing can be performed by complement dependent lymphocytotoxicity reaction (serology). Viable peripheral blood mononuclear cells are required for this assay. CD8+ T-cells and/or CD19+ B-cells are purified from whole blood and incubated against
a panel of antibodies with specificity against polymorphic epitopes expressed on HLA-A, -B and -C proteins (CD8+ T-cells) or HLA-DR and -DQ proteins (CD19+ B-cells). In the presence of complement cells expressing HLA, proteins which react with a particular antibody are lysed, allowing these damaged cells to uptake a stain which is detected by fluorescent microscopy. The pattern of negative and positive reactions is scored and interpreted to give a serological HLA type.

At present all patient and potential matching donor samples (HSC and renal transplant) are typed by HLA serology and DNA based typing. Serological HLA typing is the quickest method to establish identity within a family, and it also allows the identification of null alleles (HLA alleles detected by DNA techniques, which do not result in protein expression) when further DNA-based typing is performed.

5.1.3 DNA based typing Techniques

5.1.3.1 Sequence Specific Oligonucleotide Probe (SSOP) testing

This method is used to type all patients, related donors and unrelated donors for HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQA1 and -DQB1. We aim for all newly recruited donors to be tested for HLA-A, -B, -C, -DRB1, -DQA1, -DQB1, -DPA1 and -DPB1. The SSOP assay involves the incubation of locus specific polymerase chain reaction (PCR) products (e.g. HLA-A) with a panel of immobilised oligonucleotide probes with sequences complementary to polymorphic sequences within the HLA alleles. We are currently using Luminex® xMAP® in which the oligonucleotide probes are immobilised on polystyrene microspheres (or beads). Reactivity between PCR product and beads is detected by the measurement of fluorescence at two wavelengths, the first to identify the specificity of the bead and the second to determine if PCR product has bound.

5.1.3.2 Sequence Specific Primer (SSP) testing

SSP typing utilises a panel of PCR primer pairs which target known polymorphic nucleotide motifs within HLA alleles. The presence or absence of a PCR product (in the
presence of a positive internal control PCR product) determines the presence or absence of a particular nucleotide sequence. This pattern is interpreted to give the HLA type. -SSP is used to provide a fast ‘on-call’ HLA type of cadaveric solid organ donors. It is also used to resolve ambiguities arising from other methodologies and to confirm unusual associations between alleles in an individual (e.g. HLA-B/C associations).

5.1.3.3 PCR-Sequencing-Based Typing (SBT) testing

Direct sequencing of PCR products is performed on an automated DNA sequencer using dusterminator chemistry. Sequencing is used mostly to determine HLA-A, -B, -C, -DRB1 and -DPB1 at high resolution type for haematopoietic stem cell patients and their selected unrelated donors. Sequencing is also used to resolve any novel alleles detected by other methods. Any unacceptable ambiguities arising from sequencing are resolved by SSP.

5.2 Virology and blood group typing

Human sera are screened for the presence of CMV (antibody), HIV1/2 (antibody/antigen), hepatitis B (antigen) and C (antibody) infection by ELISA. Any ambiguous/equivocal results may be confirmed by referral to the CPA accredited Department of Virology at Royal Free Hospital, Pond Street, London NW3 2QG.

Blood group typing is performed by haemagglutination reaction to detect red blood cell antigens. Any ambiguous/equivocal results may be confirmed by referral to the CPA accredited Blood Transfusion team at Royal Free Hospital, Pond Street, London NW3 2QG.

5.3 Antibody screening

Luminex technology is used to establish the presence and specificity of HLA class I and II reactive antibodies in both pre- and post transplant patients.

Luminex

Luminex® technology uses fluorescent Microbeads coated with purified HLA class I and II proteins. The beads are incubated with patient sera and bound antibodies detected after reaction with a fluorescently labelled IgG specific secondary antibody. Test sera are screened to initially determine the presence of HLA class I or II specific antibodies. Sera scoring positive for HLA specific antibodies are further analysed with Luminex kits designed to define HLA specificities. Highly sensitised patients with IgG antibodies reactive with multiple HLA class I or II antigens are further characterised with Luminex beads possessing immobilised recombinant single class I or II molecules. This provides the highest resolution of HLA-specific antibody analysis. Currently the laboratory uses Luminex microbead products from two different manufacturers.

5.4 Crossmatching

The purpose of the crossmatch (XM) test is to determine the presence of pre-formed antibodies
in a patient that are reactive with HLA antigens on donor cells. This could cause hyper acute rejection of a renal graft. Both Complement-dependent lymphocytotoxicity (CDC) and flow-cytometric (FC) tests are performed by reacting both fresh and selected historic recipient sera with separated donor T and B-cells (allogeneic XM), and recipient T and B-cells (autologous XM). The results of these tests, in conjunction with the known immunological and clinical parameters of a potential renal transplant recipient, are used to advise renal transplant surgeons on the likely risk (high, intermediate or low) of graft rejection occurring. The FC XM is recognised to be more sensitive and objective than the CDC XM and detects both complement fixing and non-complement fixing IgG antibodies. The CDC XM although less sensitive, detects both IgG and IgM complement fixing antibodies. Both CDC and FC XM can be performed simultaneously.

A virtual crossmatch may be performed if the patient has a consistently negative antibody screening history. This means that the transplant can proceed before the crossmatch results are available.

5.5 Preparation of HLA typing reports

All collected HLA typing data is interpreted independently by two different experienced laboratory staff. Data from individual tests is submitted to SOLAR, (the Anthony Nolan information management system database), and patient and donor reports are prepared after all tests requested are completed. Reports related to patients that have been typed by our Histocompatibility Laboratories (related or registry donors) are prepared by a laboratory/clinical/biomedical scientist and authorised by a Health and Care Professions Council (HCPC) registered Clinical Scientist or above. Other potential donor reports may be issued directly from the SOLAR database via the Operations department. All HLA typing data is checked for appropriate haplotype associations based on published and in-house data. Any unusual results will be checked further and sent for DNA sequence analysis if deemed appropriate.
5.6 Participation in Quality Assurance schemes

The Histocompatibility Laboratories take part in the following external quality assurance programmes and consistently achieve satisfactory results.

<table>
<thead>
<tr>
<th>Accreditation Body</th>
<th>Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK NEQAS for H&amp;I</td>
<td>1A. HLA Phenotyping</td>
</tr>
<tr>
<td></td>
<td>1B. HLA-B27</td>
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<tr>
<td></td>
<td>2A. Cytotoxic Crossmatch</td>
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<tr>
<td></td>
<td>2B. Crossmatch by Flow Cytometry</td>
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<tr>
<td></td>
<td>3. HLA antibody specificity</td>
</tr>
<tr>
<td></td>
<td>4. HLA DNA typing</td>
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<tr>
<td></td>
<td>5. HFE gene mutation</td>
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<tr>
<td></td>
<td>6. Antibody detection</td>
</tr>
<tr>
<td></td>
<td>7. HLA-B*57</td>
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<tr>
<td></td>
<td>Educational scheme</td>
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<tr>
<td>UK NEQAS for Microbiology</td>
<td>Immunity screen</td>
</tr>
<tr>
<td></td>
<td>Blood borne virus</td>
</tr>
<tr>
<td></td>
<td>Diagnostic serology</td>
</tr>
<tr>
<td>UK NEQAS for Blood Transfusion</td>
<td>ABO + RhD blood group testing</td>
</tr>
<tr>
<td>UCLA International Cell and DNA Exchange</td>
<td>Rare cell exchange</td>
</tr>
<tr>
<td></td>
<td>Novel DNA extracts</td>
</tr>
</tbody>
</table>
### 5.7 Summary of current services provided by the Histocompatibility Laboratories

The Anthony Nolan Histocompatibility Laboratories are able to provide the following genetic testing and typing services to the defined ‘users’.

<table>
<thead>
<tr>
<th>Service</th>
<th>“User”</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematopoietic stem cell transplantation</strong></td>
<td></td>
</tr>
<tr>
<td>HLA-A, -B, -C, -DRB1, -DQA1, -DQB1, -DPB1 and -DPB1 typing of potential unrelated HSC donors</td>
<td>Anthony Nolan Operations Department</td>
</tr>
<tr>
<td>Maternal &amp; Cord Blood ABO RhD blood group typing</td>
<td>Anthony Nolan Cell Therapy Centre, Nottingham</td>
</tr>
<tr>
<td>HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQB1 and -DPB1 confirmatory typing of potential unrelated HSC donors</td>
<td>External Registers, Transplant Centres</td>
</tr>
<tr>
<td>HLA typing on stored frozen potential unrelated donor DNA</td>
<td>Transplant Centres</td>
</tr>
<tr>
<td>HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQB1 and -DPB1 typing of patients and potential related HSC donors</td>
<td>Transplant Centres</td>
</tr>
<tr>
<td>HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQB1 and -DPB1 typing of non-ANT HSC donors for patients within the U.K.</td>
<td>Transplant Centres</td>
</tr>
<tr>
<td>ABO RhD blood group typing of HSC donors and patients</td>
<td>Transplant Centres</td>
</tr>
<tr>
<td>Virology screening of potential HSC donors and patients</td>
<td>Transplant Centres</td>
</tr>
<tr>
<td>Crossmatching of patients with potential HSC donor</td>
<td>Transplant Centres</td>
</tr>
<tr>
<td><strong>Solid organ transplantation</strong></td>
<td></td>
</tr>
<tr>
<td>HLA-A, -B, -C, -DRB1-DRB3, -DRB4, -DRB5, --DQB1, -DPB1 typing of liver and renal potential transplant recipients</td>
<td>Surgical and Associated Services Division, Royal Free Hospital</td>
</tr>
<tr>
<td>HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQB1 -DPB1 typing of cadaver liver and kidney donors</td>
<td>Surgical and Associated Services Division, Royal Free Hospital, United Kingdom Transplant UK Transplant</td>
</tr>
<tr>
<td>HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQB1, typing of living kidney donors</td>
<td>Surgical and Associated Services Division, Royal Free Hospital</td>
</tr>
<tr>
<td>HLA alloantibody screening and definition for patients awaiting renal transplant</td>
<td>Surgical and Associated Services Division, Royal Free Hospital</td>
</tr>
<tr>
<td>Crossmatching of liver and renal transplant recipients and donors</td>
<td>Surgical and Associated Services Division, Royal Free Hospital</td>
</tr>
<tr>
<td>24 hour, 7 day / week on-call HLA typing and crossmatching service for liver and renal transplantation</td>
<td>Surgical and Associated Services Division, Royal Free Hospital</td>
</tr>
<tr>
<td><strong>Non-transplantation services</strong></td>
<td></td>
</tr>
<tr>
<td>HLA disease associations</td>
<td>Royal Free Hospital and other related organisations</td>
</tr>
<tr>
<td>HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQB1 and –DPB1 typing for non-transplantation projects</td>
<td>Commercial and non-commercial organisations</td>
</tr>
<tr>
<td>Haemochromatosis gene (HFE) mutation typing</td>
<td>Centre for Hepatology, Royal Free Hospital, and other requesting centres.</td>
</tr>
</tbody>
</table>
6.1 Request forms

- Any samples being sent to the laboratories must correctly packaged and should show the name and address of the sender. Samples must be correctly labelled with three identifiers (see below) and a bleed date and appropriate request forms must be present. Request forms are available for the following tests:

- Patient histocompatibility testing. [Link]
- Related donor histocompatibility testing. [Link]
- Renal and liver transplant histocompatibility testing (patient and/or donor tests)
- Disease association studies
- Haemochromatosis mutation detection

Please label blood tubes with:

Full name, NHS/CHI number, Date of Birth, Hospital Number, Place, time & Date where sample was taken. Incorrectly or insufficiently labelled tubes / paperwork will result in the sample being discarded.

It is the requesting centre’s responsibility to ensure appropriate patient and donor consent as stipulated by the Human Tissue Act 2004 is obtained for the requested tests.

All details required for sample collection are on the request forms (please use block capitals).

Sample Requirements

<table>
<thead>
<tr>
<th>Test</th>
<th>Sample required</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA typing for HSCT (patient and donor)</td>
<td>2 x 4ml EDTA</td>
</tr>
<tr>
<td>Disease Associations</td>
<td>1 x 4ml EDTA</td>
</tr>
<tr>
<td>Virology screening</td>
<td>1 x 4ml clotted</td>
</tr>
<tr>
<td>Blood grouping</td>
<td>1 x 4ml EDTA</td>
</tr>
<tr>
<td>New renal/liver patient</td>
<td>40ml EDTA 1x 10ml clotted</td>
</tr>
<tr>
<td>Renal crossmatch</td>
<td>1 x 10ml clotted</td>
</tr>
<tr>
<td>Renal antibody screening</td>
<td>1 x 10ml EDTA</td>
</tr>
<tr>
<td>Renal/liver donor</td>
<td>40ml EDTA</td>
</tr>
</tbody>
</table>
All samples should be stored and shipped at room temperature. Please ensure all mailing containers are compliant with UN3373 and IATA 650 transport regulations. All pathological specimens should be packaged by a recognised laboratory or institution, a qualified medical practitioner or a dental practitioner.

6.2 Factors known to affect performance of tests

In general samples should be sent to the laboratory without delay at ambient temperature as certain tests require viable cell populations. Furthermore our ability to extract quality DNA can be reduced in old samples.

It is important to collect samples into the correct tubes. Please ensure the correct anticoagulant (usually EDTA) or no anticoagulant (clot) is used. It is also important to supply adequate volumes of blood to allow completion of testing.

Certain tests can be affected if a patient has a low white blood cell count as a result of drug treatment or disease.

Serum samples for HLA antibody screening and crossmatching must be received in the laboratory within 48 hours of being drawn. Serum must be used in downstream procedures within 48 hours of being drawn or stored at -70°C until required

For Flow and CDC crossmatching; EDTA blood used for lymphocyte isolation must be despatched at ambient temperature and reach the laboratory for processing within 48 hours of being drawn.

6.3 Histocompatibility laboratory address and opening hours

Postal address of Histocompatibility Laboratories:
The Round Table Laboratories
Anthony Nolan
Royal Free Hospital
77B Fleet Road
NW3 2EZ

The laboratories are open Monday to Friday, excluding bank holidays from 8am to 5pm. We also provide an out of hours service in support for solid organ transplantation at the Royal Free hospital.

6.4 Time limits for requesting additional examinations

Samples from all patients who have undergone a transplant and their donors (related and unrelated) are securely stored frozen in the laboratories as either DNA or whole blood in accordance with national guidelines.

Serum samples from renal and liver transplant patients (pre and post transplant) are securely stored frozen in the laboratories as sera in accordance with national guidelines.

6.5 Histocompatibility Laboratories contact details

Laboratory reception telephone number: 020 7284 8348

Laboratory fax number:
020 7284 8301

Laboratory email address (general enquiries):
laboratories@anthonylogan.org
HISTOCOMPATIBILITY LABORATORIES DEPARTMENT
SENIOR STAFF

Director of Laboratories
Consultant Clinical Scientist
Katy Latham BSc, PhD, HCPC registered, FRCPath

Co-Director of Laboratories
Professor Steven G E Marsh
BSc PhD ARCS

Consultant & Scientific Director
Professor Alejandro Madrigal
MD, PhD, FRCP, FRCPath, DSc

Laboratory Manager
Richard Holman, BSc, MSc, HCPC registered

Consultant Clinical Scientist
Henry Stephens, BSc, PhD, HCPC registered

Section Leads
Finnuala A Fowles, BSc, HCPC registered (Intermediate Typing Lead)

Joyce Grant, BSc, MSc, HCPC registered (Solid Organ Group Lead)

Helen Ogilvie, BSc, HCPC registered (Clinical Services Customer Lead)

Anila Shah, BSc, HCPC registered (Register Reporting customer Lead)

Franco Tavarozzi, BSc, HCPC registered (High Resolution Typing & Commercial Lead)

Salmah Mahmood, BSc, LIBMS, HCPC registered
Head of Quality (Quality Manager)
8 The Future

1. To continue to provide an excellent Histocompatibility and Immunogenetics service for patients in need of a stem cell transplant.

2. To continue to increase the number of donors recruited and HLA typed on our register.

3. To increase laboratory automation.

4. To increase the level of resolution performed for register HLA typing, thus minimising time required to identify and perform confirmatory typing.

5. To increase the resolution of the HLA typing performed on patients and potential matched donors whilst maintaining desired sample turnaround times.

6. To promote closer collaboration with transplant centres in order to assess their needs and to maintain an effective and efficient service.

7. To establish additional genetic testing services to improve donor and patient matching in haematopoietic stem cell transplantation and other clinical procedures.

8. To continue our research programme and analysis of our donor database so that we can better understand the diversity of donor phenotypes which will enable us to specifically select donors at an early stage for whom further typing will be useful.

9. To maintain and improve the quality of Histocompatibility and Immunogenetics service provided to support the solid organ transplant programme of the Royal Free Hospital, London.

10. To maintain compliance with laboratory accreditation via Clinical Pathology Accreditation (UK) Ltd. and European Federation for Immunogenetics accreditation.

11. To maintain regulatory compliance with the Human Tissue Authority (HTA) and the Care Quality Commission (CQC).
If you wish to make a formal complaint regarding the services provided by the Anthony Nolan Histocompatibility Laboratories, or to report a Serious Adverse Event or Reaction (SAER), please send details in an email to the Quality Team: QualityTeam@anthonynolan.org