Desa Lilic and Mario Abinun
Gift Donation
For the advancement of Clinical Immunology in Serbia

Signing of Gift Donation - summer 2019

The Purpose:

The Gift Donation made to Newcastle University will enable and enhance the practice and advancement of clinical immunology in Serbia, specifically:

- adult and paediatric clinical immunology
- clinical immunology diagnostic services
- clinical immunology research.

This will be achieved by supporting reciprocal exchange of knowledge, visits, interactions and forging of contacts between candidates from Serbia and candidates from Newcastle, UK.

Funding:

Recipients will receive up to 3000GBP in a single instalment for a maximum duration of 6 months. The support and duration are flexible but must be justified in the project proposal. Possible changes are at the discretion of the Selection Panel (see below).

Candidates:

- Eligible candidates include medical staff/clinical scientists/scientists /academics working in the field of clinical immunology, prioritising primary immune deficiencies (PIDs) but not excluding other areas of clinical immunology/immune pathology.
- Candidates will either be from Serbia coming to Host Institutions in Newcastle or from Newcastle going to Host Institutions in Serbia. There is no age restriction, but candidates established in their field will have preference.

Host Institutions:

- In Newcastle: Newcastle University Faculty of Medical Sciences and linked NHS Teaching Hospitals in Newcastle and the North East
- In Serbia: Medical Faculties at accredited Universities and linked teaching hospitals throughout Serbia (presently in Belgrade, Novi Sad, Nis, Kragujevac).

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Activities:

- For candidates coming from Serbia to Newcastle Host Institutions:

- candidates (medical staff including doctors, nurses, technicians etc) attending as visiting clinical observers to participate in patient care, management and accreditation of clinical services, prioritising Primary Immune Deficiencies (PIDs) both adult and paediatric, but not excluding other areas of clinical immunology
- candidates visiting clinical diagnostic laboratories to acquire new skills, novel diagnostic techniques, new technologies and management including quality control and accreditation
- candidates participating in ongoing research projects relating to PIDs
- acquiring equipment and/or reagents for the advancement of research and/or diagnostic procedures in clinical immunology laboratories in Serbia (excludes consumables for routine work)

- For candidates from Newcastle going to Serbian Host Institutions:

- organising workshops and training courses in Serbia
- organising and setting up standardisation procedures, quality control schemes and promoting accreditation of clinical and laboratory services in Serbia
- candidates from Newcastle to take part in ongoing research projects in Serbia

Application process:

- Submission of a project proposal with clearly defined aims, objectives and outcome measures
- Anticipated impact for the advancement of clinical immunology
- special consideration will be given to projects promoting collaboration of clinical/ diagnostic/ research aspects of clinical immunology

Selection Panel:

A panel will be formed by the Newcastle Host Institutions, which will comprise of:

- Adult and paediatric clinical immunologists (medical doctors and nurses) and/or
- Clinical Scientists in diagnostic laboratories relevant to clinical immunology and/or
- Scientists/ academics conducting research in the field of clinical immunology

Final Report

- A Final Report will be submitted within 6 months of project completion to the Selection Panel and Host Institution for assessment against anticipated objectives and outcomes. The report will be posted on this website for public access and comments

Application process

- Application forms will be available on The Faculty of Medical Sciences, Newcastle University website (https://www.ncl.ac.uk/medicalsciences/) in early spring 2020 with a decision date anticipated for May 2020 (dates to be confirmed).

Why have Desa & Mario set up this donation?

DL and MA qualified as medical doctors at Belgrade and Sarajevo University respectively (former Yugoslavia).

Prior to moving to the UK in 1992, DL worked at the Military Medical Academy (MMA) where she specialised in Clinical Immunology and conducted research under the guidance of Col Dr Aleksandar Dujic. MA specialised as a paediatrician at the Institute for Mother and Child Health Care under Dr Mirko Mikuska.

From the very beginning, both DL and MA focused their clinical and research interests on immunology and were active participants of the then (and now) prestigious Yugoslav Immunology Society led by Professors Mirko Simic and Miodrag-Mija Lukic. and were founding members of the newly formed European Society for Immune Deficiency (ESID) which is now internationally renowned.

In 1990, under the guidance of Professor Roland Levinsky and Dr Gareth Morgan from Great Ormond Street Hospital, London, MA and his team conducted the first bone marrow transplantation (BMT) in a child with severe combined immune deficiency (SCID) in former Yugoslavia, where the bone marrow was prepared by DL and her team at the MMA.

In 1992, they were invited by Professor Roland Levinsky to come to Newcastle, MA to the newly set up NHS paediatric BMT Unit with Professor Andrew Cant, while DL set up her research at Newcastle University with the help pf Dr Gavin Spickett and Professor Jane Calvert. DL also set up and headed Clinical Immunology Diagnostic Laboratories at the James Cook University Hospital in Middlesbrough and University Hospital of North Durham and set up specialised Candidiasis clinics at the Royal Victoria Infirmary in Newcastle for patients with Chronic Candidiasis which were the focus of her academic research.

MA made significant contributions in the treatment and diagnosis of PIDs. He also set up BMT in children with juvenile arthritis and other systemic autoimmune diseases.

- Antoine C et al (EBMT/ESID). Long-term survival and transplantation of haemopoietic stem cells for immunodeficiencies: report of the European experience 1968-99. Lancet. 2003;361(9357):553-60.
- Döffinger R et al. X-linked anhidrotic ectodermal dysplasia with immunodeficiency is caused by impaired NF-kappaB signaling. Nat Genet. 2001;27(3):277-85.
- Angulo I et al. Phosphoinositide 3-kinase δ gene mutation predisposes to respiratory infection and airway damage. Science. 2013;342(6160):866-71.
- Cuchet-Lourenço D et al. Biallelic *RIPK1* mutations in humans cause severe immunodeficiency, arthritis, and intestinal inflammation. Science. 2018;361(6404):810-13.
- Abinun M et al. Autologous T cell depleted haematopoietic stem cell transplantation in children with severe juvenile idiopathic arthritis in the UK (2000-2007). Mol Immunol. 2009;47(1):46-51.
- M F Silva J et al (Abinun M **shared co-senior authorship**). Allogeneic hematopoietic stem cell transplantation for severe, refractory juvenile idiopathic arthritis. Blood Adv. 2018;2(7):777-86.

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DL made significant research and clinical contributions in the identification of underlying mechanisms in the 2 largest cohorts of PID patients presenting as Chronic Mucocutaneous Candidiasis (CMC):

- in one cohort of CMC patients, the identification of an underlying STAT1-gain of function mutation
    - van de Veerdonk FL et al. (Lilic D **shared co-senior authorship**): Mutations in the CC-domain of STAT1 in Autosomal Dominant Chronic Mucocutaneous Candidiasis. New Engl J Med 2011,365 (1):54-61;
    - Toubiana J et al (on behalf of the International STAT1-GOF study group): STAT1 gain of function mutations underlie an unexpectedly broad clinical phenotype: an international survey of 274 patients. Blood 2016;127(25):3154-3164
- in a second cohort of CMC patients with the AIRE gene mutation, the existence of anti-IL-17 antibodies which explained the link between autoimmunity and immune deficiency
    - Puel A et al. (Lilic **shared co-senior authorship);** Auto-antibodies to IL-17A, IL-17F and IL-22 in patients with chronic muco-cutaneous candidiasis and auto-immune polyendocrine syndrome type I. J Exp Med 2010; 207:291-297 (**Editorial:** Maxmen A. Antibodies attack IL-17. J Exp Med 2010;207(2):264-5);
    - Kisand K, Lilic D, Casanova JL, Peterson P, Meager A, Willcox N. Mucocutaneous candidiasis and autoimmunity against cytokines in APECED and thymoma patients: clinical and pathogenic implications. Eur J Immunol 2011; 41:1517-1527.

These findings enabled not only identification of the disease, but as well novel diagnostic approaches and new treatments in these patients

- Meloni A et a. Autoantibodies against type I interferons as an additional diagnostic criterion for autoimmune polyendocrine syndrome type I. J Clin Endocrinol Metab. 2008;93(11):4389-97;
- Higgins E et al (Lilic D **shared co-senior authorship);** Successful treatment of a patient with Chronic Mucocutaneous Candidiasis due to a gain-of-function STAT1 mutation with the JAK1/2 inhibitor ruxolitinib. JACI 2015,135 (2):551-553;
- Forbes LR et al..Jakinibs for the Treatment of Immunodysregulation in Patients with Gain of Function STAT1 or STAT3 Mutations. JACI 2018, 142(5):1665-1669;

Given their careers, commitments and enduring passion to understand immune mechanisms in clinical immunology practice, particularly PIDs, DL and MA were keen to contribute and support further advancement of all aspects of Clinical Immunology in Serbia where they trained and initiated their interests in this exciting field.

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