2. BACKGROUND – THE IMMUNOLOGY TRAINING PROGRAM (ITP) AT UAB 2A. Rationale

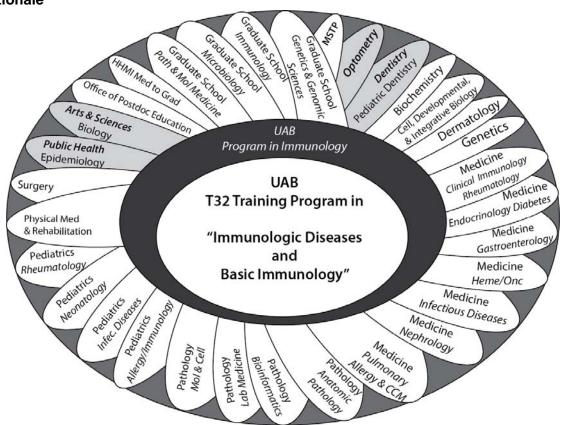


Figure 1. This T32 Training Program lies at the heart of the Program in Immunology and brings together faculty representing five Schools, 22 Departments and 15 Divisions (not all are shown).

The multidisciplinary UAB Immunology Training Program, "Immunologic Diseases and Basic Immunology", is focused on training highly motivated pre-doctoral students and PhD and MD graduates in the fields of translational and fundamental immunology. The primary focus of UAB's immunology research remains the elucidation of pathogenic mechanisms operative in diseases of immune etiology. Our trainees are selected for their commitment to research and academic medicine. The success of their future investigator-initiated studies, which are best represented by R01-caliber projects, requires the development of skilled creativity and the ability to identify and achieve scientific goals of significance to the biomedical research enterprise. UAB has a longstanding commitment to the fields of fundamental and clinical immunology, and this support continues with Immunology, Autoimmunity and Transplantation acknowledged as one of the six pillars at the heart of our school-wide Strategic Plan in close association with a second pillar, Infectious Diseases and Host Defense. To provide an effective interdisciplinary training environment, this program builds on the interdisciplinary basic and translational investigative efforts supported by the UAB Program in Immunology (Appendix D). This University-wide program spans five schools, 22 departments and 15 divisions and in August of 2012 included 125 faculty members, the core of which, 57 faculty members, serve as mentors on this training program. This represents an increase of 20 faculty members since 2006. Key partners are the thematically based UAB Graduate Biomedical Sciences program (Appendix A), the UAB MSTP (MD/PhD) program (Appendix A), the Office of Postdoctoral Education (Appendix B), and the Rheumatology and Allergy/Immunology Fellowship Programs (Tables 7B & 8B). The ITP incorporates an established faculty committed to training in the fields of fundamental and translational immunology and consistently adds new faculty who bring both new perspectives and expertise. It makes the explicit effort to incorporate and mentor young faculty to further strengthen a strong mentoring environment and to promote development of all phases of training. An effective interdisciplinary training program requires faculty with collaborative and synergistic scientific interests and coordinated training opportunities. The strong research environment at UAB, embodied in the Program in Immunology, provides a foundation for collaborations. This is exemplified by the coauthorship of manuscripts by our faculty mentors. Of their publications identified in PubMed during the last 10 years, 91% of the faculty mentors collaborated with at least one other mentor; 69% collaborated with three or more mentors, and 14% collaborated with nine or more different mentors during this period. Moreover, 49% of the pre-doctoral trainees and 44% of the post-doctoral trainees published with two or more Faculty mentors. This history of collaborative and productive publication illustrates this T32 Training Program in Immunologic Diseases and Basic Immunology is the heart of the UAB Program in Immunology (Figure 1). This committed training environment provides an ideal setting for the implementation of interdisciplinary research and training in a broad range of immunologic diseases and in fundamental and translational immunology.

We are requesting continuation of support for 10 pre-doctoral and, per the recommendations of our previous study section, 3 post-doctoral trainees. Based on our past record of 100% enrollment, the increase in our applicant pool (Tables 7A and 7B), and our expanded pool of highly collaborative mentors, we believe this request is fully justified. Over the past five years, 23 predoctoral and 16 postdoctoral trainees have been supported, with 36 of 39 (92%) continuing as faculty members, teachers in K-12 education. administrative or research staff positions (academic staff), and/or continued academic training. Of the 30 mentees pursuing additional academic training, 21 are continuing various training paths at UAB. The nine remaining mentees are pursuing training at the La Jolla Institute of Allergy and Immunology, Medimmune, University of Pennsylvania, Northwestern, Tufts, Johns Hopkins, NIH, Baylor, and Duke. [The three postdoctoral trainees who are engaged in other activities include one pharmacologist at FDA/CDER, one inspector for the FDA and one scientific writer.] Our trainees in this period have been 41% male and 59% female; and have included 18% under-represented minorities (15% African American, 3% Native American) (Table 11). They have trained with 31 different primary or co-mentors from five different departments (Cell, Developmental & Integrative Biology, Medicine, Microbiology, Pathology, Pediatrics and Physiology & Biophysics) and 10 divisions. These trainees have published 110 peer-reviewed manuscripts, averaging 3.8 papers per predoctoral trainee who graduated and 2.7 papers per post-doctoral trainee who completed their T32 support (see Tables 6A/6B and section 6). Of these, 20% were published in journals such as Science, Nature, Nature Immunology, Immunity, the Journal of Experimental Medicine, the Journal of Biological Chemistry, the Proceedings of the National Academy of Sciences USA, Annual Reviews of Immunology, Nature Reviews in Immunology, Current Opinion in Immunology, Trends in Immunology, and Seminars in Immunology.

2B. Historical Background

In 1976, UAB was first awarded this Institutional NRSA (T32 AI 007051) to support a training program in Allergic and Immunologic Diseases and Basic Immunity. At its inception under the directorship of Robert Stroud MD, the program focused on basic pathogenic mechanisms and translational studies. Following the departure of Dr. Stroud in 1979, John E. Volanakis MD assumed directorship of the program. In 1991 Max D. Cooper MD became the director of the program, with the aid of Harry W. Schroeder MD PhD, who served as Associate Director. Upon Dr. Cooper's retirement from UAB in 2007, Dr. Schroeder was named Director and Laurie Harrington PhD, an ITP graduate, was named Associate Director. Over the past 35 years of support, the interests of the program have expanded to create a rich basic and translational environment, outlined below.

Research opportunities directly related to <u>human diseases</u> are available in the following areas: primary and acquired immunodeficiencies, autoimmune diseases, inflammatory diseases of the gut, microbial pathogenesis, neoplastic diseases, immune-complex diseases, immunologic disorders of the skin, host-defense defects, allergy, asthma, dental caries, transplantation, vaccinology and bioinformatics.

<u>Basic research</u> opportunities are also available in: lymphoid cell differentiation from the stem cell to the terminally differentiated lymphocyte, structure and function of immunoglobulins and T cell receptors, transplantation immunology, neuroimmunology, biochemistry and biology of complement, Fc and Fc-like receptors, immunoglobulin and T cell receptor gene utilization during ontogeny and phylogeny, secretory immunity, structure and function of lymphokines, the ontogeny and function of T cell subsets such as TH17 cells and cytotoxic lymphocytes, biosynthesis of autoantibodies and bioinformatics.

In 2003, in recognition of the continued growth of immunology research on campus, UAB created the Program in Immunology to help coordinate the wide distribution of immunology-related research at UAB. The goal of this trans-departmental program is to enhance communication among faculty and immunology trainees in order

Immunology Training Program and the UAB Program in Immunology, Dr. Schroeder was named as the Director of the UAB Program in Immunology in 2008. Building on established strengths, Dr. Schroeder undertook a reorganization of both the Program in Immunology and the Immunology Training Program through the creation of overlapping workgroups, which provide the intellectual framework for research, training and service. These workgroups provide focus within these two broad programs and highlight the opportunities for integration and interdisciplinary research. At the level of research and training, the workgroups are reflected in the form of work-in-progress seminars and journal clubs, which currently include Allergy and Clinical Immunology, Autoimmunity, Cellular and Molecular Immunology, Inflammation, Neuroimmunology and Mucosal Immunology. These workgroups combine efforts in fundamental, translational and clinical immunology. During the past five years of support, this training program has added 26 new mentors to replace the eight previous mentors who have retired, left the institution, or changed their field of interest bringing in new expertise. The overlapping research and training interests of the faculty facilitate co-mentorship, which extends to the coupling of fundamental and translationally-oriented mentors. This approach has strengthened the training program emphasis on an interdisciplinary didactic curriculum, on professional development (including a new graduate level (MIC741) course developed by Drs. Schroeder and Harrington and specific to our T32; Appendix C) and on the process of mentoring both the mentors and the trainees. This emphasis is embodied in the participation of the program faculty as course masters, module leaders and lecturers in the GBS themes of Genetics and Genomic Sciences, Immunology, Microbiology, and Pathobiology/Molecular Medicine. These initiatives have occurred in the context of the University-wide emphasis on collaboration, cooperation, and interdisciplinary efforts to translate research from the bench to the bedside and to provide access to the latest technologic approaches, including computational biology, bioinformatics and genomics. Over the last five years, 23 pre-doctoral and 16 postdoctoral trainees have been supported, with 36 of 39 (92%) continuing as faculty members, teachers in K-12 education, administrative or research staff positions (academic staff), and/or continued academic training. Of the 30 mentees pursuing additional academic training, 21 are continuing various training paths at UAB. The nine remaining mentees are pursuing training at the La Jolla Institute of Allergy and Immunology, Medimmune, University of Pennsylvania, Northwestern, Tufts, Johns Hopkins, NIH, Baylor, Duke. [The three post-doctoral trainees who are engaged in other activities include one pharmacologist at FDA/CDER, one inspector for the FDA and one scientific writer.] Our trainees in this period have been 41% male and 59% female; and have included 18% under-represented minorities (15% African American, 3% Native American) (Table 11). This compares to the previous five year period where the trainees were 60% male and 40% female, and 9% under-represented minorities (6% African American and 3% Hispanic American). This program has made a broad and systematic effort to include the best trainees and mentors interested in immunology research. Over the past five years, they have trained with 31 different primary or co-mentors from five different departments (Cell, Developmental and Integrative Biology, Medicine, Microbiology, Pathology, and Pediatrics) and 10 divisions. Over the past ten years, our students and postdoctoral fellows have trained with mentors in eight Departments (Cell Biology, Genetics, Medicine, Microbiology, Ophthalmology, Pathology, Pediatrics and Physiology & Biophysics). We believe that this interdisciplinary breadth creates a rich investigative training experience for trainees and faculty alike.

to identify and stimulate additional synergies across campus. To facilitate the integration between the

2C. Need for Training

Many organizations, including the Association of American Medical Colleges, the American Association of Immunologists, and the Immune Deficiency Foundation, have identified the training of investigators and the development of young faculty prepared for the rapid advances in biomedical knowledge and health care delivery, as one of the highest priorities for the continued development of academic medicine and, specifically, the research mission in the diseases of immune function. The training of a cadre of investigators, -- physician/investigators, PhD scientists, and translational scientists (with or without clinical training) all of whom are at the interface between immunologic diseases and mechanisms of disease pathogenesis -- is critical to future advancements in the understanding and treatment of immunologic diseases. We believe that rigorous training in research methods and a strong appreciation for interdisciplinary challenges and opportunities are critical for a career in academia and biomedical investigation. The heightened awareness of the interdependence of clinical and more fundamental scientists and a basic understanding of pathophysiologic

mechanisms and molecular techniques will help inform research initiatives, not only at the bench but also in the clinic. This understanding is also essential for the application of new diagnostic technologies and therapeutic modalities that are now reaching into the effective practice of medicine.

The training program faculty and the interdisciplinary environment fostered by the Program in Immunology at UAB positions our trainees at the intersection between mechanism-based research, its application to clinical medicine, and its impact on disease outcomes. Our training record, as exemplified by the pre- and post-doctoral trainees not only in the last five years but over the previous 30 years (Appendix F) emphasizes our strong commitment to trainees with a reciprocal commitment to careers in investigation (of 142 trainees supported between 1976 and 2006 inclusive, 60 (42%) have academic faculty positions, 19 are in biotechnology, 9 have non-tenured positions at the NIH or other research institutions, 17 are still in training, 26 are in private clinical practice, 3 are high school teachers, 1 is a medical technologist, and 7 are lost to current follow-up). The new opportunities developed within the School-wide Strategic Plan, and embodied in new initiatives within the Graduate Biomedical Sciences Program and the Program in Immunology, have underscored the critical role of training positions for pre-doctoral candidates and postdoctoral trainees. In this renewal application, therefore, we are asking for continued support for previously awarded 10 pre-doctoral positions and a reduction from support for 5 to 3 postdoctoral training positions, as recommended by the previous study section.

2D. Relationship of the Proposed Program to Current UAB Activities

For post-doctoral candidates seeking clinical training in immunologic diseases, the first clinical year of the program, paid for by institutional funds, focuses on an intensive clinical experience based on outpatient, inpatient, and consultative evaluation and management of patients with immunologic and rheumatic diseases. Following the clinical experience, trainees devote two to three years to intensive research training, structured around a mentored research project and a didactic curriculum. For candidates without clinical training, the program consists of three to four years of intensive research training. To extend the impact of our training support, we have encouraged all trainees to seek extramural support in an appropriate and timely fashion and have had success with various foundations and associations, as well as with individual NIH awards.

Our current program (2007-2012) has developed several key initiatives:

We have instituted a formal co-mentorship program designed to broaden the training experience through a translational perspective and to provide content focus on the immunologic diseases. Typically, the program brings together mentors with and without clinical training.

With the reorganization of our School-wide graduate program into thematic areas, including Immunology, we have developed a new T32-specific course "Topics in Professional Development" (MIC741), which is required of all of our trainees, and several new Journal Clubs (Autoimmunity, Cellular and Molecular Immunology, Mucosal Immunology, Inflammation, Neurodegenerative Diseases, and Neuroimmunology) which are taken by our trainees to meet their credit requirements. In addition, we have developed two disease-specific Journal Clubs – Rheumatology and Allergy/Clinical Immunology, organized by our training faculty (Raman and Atkinson), to emphasize the bridge between fundamental and clinical/translational science.

To enhance our emphasis on both immunologic diseases and basic immunology, we have added 26 new faculty faculty (Drs. Almeida, Brown, Cron, Deshane, DeSilva, Fujihashi, George, Goepfert, Harrington, Hatton, Hughes, Hsu, Kabarowski, Katz, Lefkowitz, Li, Lund, P Mannon, R Mannon, Pasche, Randall, Schwiebert, Shalev, Smythies, Steele and Tse). These faculty support new and enhanced areas of emphasis within the Program in Immunology, reflecting our commitment to rigorous research training in these areas and new opportunities provided by extramurally funded grants and program projects. The newly recruited faculty have provided increased programmatic emphasis on interdisciplinary research to effectively interpret the impact of our new knowledge of basic immunology on the pathogenesis of a wide range of immunologic diseases. Opportunities in clinical research have been afforded by funded extramural programs such as the Center for Clinical and Translational Sciences (CCTS), the Comprehensive Diabetes Center (CDC), the Comprehensive Cancer Center (CCC), the Center for Education and Research in Therapeutics (CERTs), the Program Project in SLE, and the CLEAR Registry for Outcomes in Rheumatoid Arthritis.

Reflected in the required T32-specific "Topics in Professional Development" course is the commitment of University leaders, including the Dean, the Chairs of the major departments within the Program in Immunology

as well as its leading faculty, to our training program and its increased focus on mentoring not only pre-doctoral but also post-doctoral trainees. This includes structured practice with feedback in oral and poster presentations, in grant writing, in manuscript preparation and in career planning.

In developing the proposed program, the Program Director, the Executive Committee and the Program Faculty have carefully considered guidelines for graduate students and postdoctoral trainees, including reports of the National Academy of Sciences and the National Institutes of Health. We feel strongly that clear training goals and benchmarks for progress and success are an essential component of our responsibility for effective mentoring of trainees and support of career development. Below are a few examples of the outcomes of some of the initiatives described above:

- (1) Program in Immunology. Our School-wide Strategic Plan for Research, initially presented in 2006 and revised through an ongoing School-wide effort in 2011, is fully committed to fostering the development of pre-doctoral trainees, post-doctoral trainees and faculty. Our trainees serve as official hosts and meet for lunch and a literature discussion/mentoring session with on-campus visitors coming for the Program in Immunology Seminar Series. They also serve as trainee representatives in the major administrative subgroups of the Program, which provides them with a broader perspective of the opportunities for service and leadership that are an integral part of the academic experience.
- (2) **Trans-disciplinary UAB-based coursework**. The training program faculty have initiated several new graduate courses emphasizing the development of knowledge from bench to bedside and back. Experimenting with different teaching and participation formats and intentionally creating student work groups of PhDs and MD/PhDs, our training faculty have stressed the inter-relatedness of immune-based studies (e.g. MIC778-Primary Immune Deficiencies, MIC740/CB745-Protective and Pathogenic T cell Responses, GBS743-Innate Immunity, and MIC700 Advanced Course in Autoimmunity). Pre-doctoral trainees take at least one of these courses; post-doctoral trainees are highly encouraged to participate.
- (3) Enrichment with off-campus coursework. Over the last five years, we have placed additional emphasis on off-campus educational opportunities. We have had faculty and trainees participate in AAI and CIS Immunology courses, in addition to local, regional and national meetings to present research findings. For example, Ms. Ewa Szymanska participated in the AAI 2011 Advanced Course in Immunology. These experiences will continue to complement on campus coursework by helping tailor the training experience to meet each trainee's individual needs and interests.
- (4) **Pathways for translational research**. The translational emphasis of this T32 training program is strongly supported by the institution in several ways.
 - a. **HHMI-sponsored "Med into Grad" Program**. Designed to provide PhD students with a more targeted exposure to human biology and disease (Halpert), we leverage coursework developed for this program (**Appendix A**).
 - b. **MD/PhD training**. We recruit pre-doctoral students from our MD/PhD program (e.g., George Atkinson, Kayci Huff, Daniel Schreeder).
 - c. **Allergy/Immunology** and **Rheumatology Fellowship Programs**. We recruit post-doctoral trainees from our immunology-oriented clinical fellowship programs (e.g. Dr. John Anderson, now an Assistant Professor of Medicine, and Dr. Tracy Hwangpo).

2E. Institutional Support of Research Training

In addition to providing support for training in the first clinical year, the University, School and Faculty Practice have provided substantial support for the development of a research training infrastructure as exemplified in the new Graduate Biomedical Sciences programs, in the Office of Postdoctoral Education and in undergraduate research experiences, in addition to the activities of the Department of Medicine's Mentors' Advisory Committee. Each of these efforts provides complementary support for research career development. Institutional funds are available to support matching travel awards for trainees to the AAI and FOCiS sponsored training programs. Trainees are encouraged to attend on-campus enrichment workshops such as the Opportunities in Immunology workshop series, Seminars in Statistical Genetics (e.g., 1st Short Course on Statistical Genetics and Genomics and Workshops in Genomic Technologies). For postdoctoral trainees, the Center for Clinical and Translational Science (UAB's CTSA) provides competitive funding for pilot research grants by scientists and physician/investigators to facilitate the transition to junior faculty positions. The Department of Medicine supports salary and research expenses for at least two physician/scientists each year, on a competitive basis, through the Frommeyer Program aiding in the transition to junior faculty positions.