


PEOPLE & IDEAS

Charles E. Egwuagu: Going with the flow

Stephanie Houston 

Charles E. Egwuagu is an epidemiologist/immunologist and chief of the Molecular Immunology Section at the National Eye Institute, National Institutes of Health, Bethesda, MD. His laboratory is focused on understanding the role played by lymphocytes in autoimmune diseases of the central nervous system. I chatted with Charles about his career so far.

Where did you grow up?

I was born in Owerri, Nigeria, and my parents emigrated to Cameroon, West Africa when I was 1 yr old. We lived in the coastal city of Victoria (renamed Limbe) in the Southwest region of Cameroon. I received my early education at the Roman Catholic Primary School in New Town, Victoria.

When did your interest in science begin? What was your first experience of science?

My interest in science began at St. Joseph's College Sasse, West Cameroon, an all-boys boarding school founded by Catholic Jesuits of the Mill Hill Missionaries. Based on British colonial government policy to promote STEM in its colonies, I qualified for the high school program focused on science careers. Although I loved chemistry and physics, my passion was in biology, particularly hygiene.

Where and with whom have you studied (undergraduate, graduate, postdoc)?

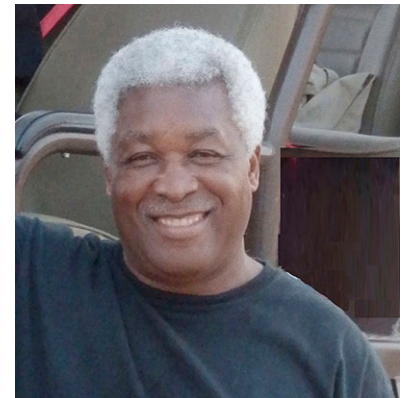
After completion of my General Certificate of Education curriculum, I immigrated to the United States at the age of 19 to further my education. I received a BA in biology (Kean University, Union, NJ) and MS in biochemistry (Rutgers University, New Brunswick, NJ). It was then that I rekindled my passion for hygiene, with specific interest in infectious and tropical diseases. I enrolled in the Yale School of Public Health and the Yale Graduate School, where I received an MPH in infectious diseases (parasitology and virology) and public health. I

also received an MPhil and PhD in epidemiology and microbiology.

I was very fortunate to have excellent mentors during my graduate education and postdoctoral fellowship. My graduate school thesis advisor at Yale was Dr. Curtis L. Patton (professor of epidemiology and one of the few tenured African-American professors at the Yale School of Medicine). Dr. Nancy Ruddle, professor of immunology and epidemiology, was a member of my thesis committee whom I admired and who would later introduce and recommend me to my postdoctoral advisor/mentor at the National Institutes of Health (NIH), Dr. Igal Gery. I am also indebted to Dr. Keiko Ozato (NIH), who introduced me to research on the interferon regulatory factor family of transcription factors and invited me to work in her laboratory, where I gained valuable training in analysis of transcription factors and transcriptional regulation. Finally, Dr. Ana Chelinsky is another mentor with whom I published several insightful papers on the role of interferon regulatory factors in lens development.

What interested you about your current area of study?

My first and only job since leaving Yale has been at the National Eye Institute of the NIH. I came to the NIH as a staff fellow in the Laboratory of Immunology and later as a commissioned officer of the US Public Health Service. My initial work in the laboratory of Dr. Igal Gery, the eminent immunologist and discoverer of IL-1, led to the seminal discovery of the molecular basis of



Charles E. Egwuagu

susceptibility to organ-specific autoimmune diseases. In a 1997 *Journal of Immunology* Cutting Edge paper, we provided evidence that the level of thymic expression of autoantigens correlates with susceptibility or resistance to autoimmune disease. Thus, resistance to an organ-specific autoimmune disease is regulated by capacity to establish central tolerance to the relevant autoantigen. (Egwuagu et al., 1997). Subsequent studies to identify autoreactive lymphocytes that mediate uveitis culminated with our finding demonstrating the critical role of Th17 cells in the etiology of human autoimmune diseases, such as uveitis and scleritis. Additional studies after the publication of our 2007 *Nature Medicine* paper (Amadi-Obi et al., 2007), convinced us of the need to refocus our research on developing biologics and cell-based therapies that can be used to target pathogenic lymphocytes that cause autoimmune diseases.

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What are you currently working on? What is up next for you?

Research in my laboratory aims to understand molecular and cellular mechanisms that cause or regulate the development of organ-specific autoimmune disease such as uveitis or multiple sclerosis. Particular focus is on (i) mechanisms that regulate lymphocyte development and cell-fate decisions; (ii) identifying and characterizing lymphocyte subsets that mediate or suppress central nervous system (CNS) autoimmune diseases; and (iii) developing biologics and cell-based therapies for CNS inflammatory diseases, such as uveitis, multiple sclerosis, and age-related macular degeneration. Our work on the immunobiology of IL-12 family cytokines and their role in lymphocyte differentiation and regulating the intensity and duration of immune responses led to our discovery of novel regulatory B cell (Breg) populations that suppress inflammation through production of IL-27 (i27-Breg) or IL-35 (i35-Breg; Wang et al., 2014). Our recent studies on the immunobiology of IL-27 or IL-35 cytokine revealed that each of the α and β subunit of IL-12 family cytokines, e.g., IL-12p35 or Ebi3, possesses intrinsic immunoregulatory functions that we are now exploiting therapeutically (Dambuza et al., 2017). Together, these studies have formed the basis of our long-term goal to develop i27-Breg and i35-Breg immunotherapies for the treatment of CNS autoimmune and neurodegenerative diseases and chronic graft-versus-host disease.

What kind of approach do you bring to your work?

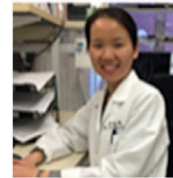
I maintain an environment that promotes intellectual curiosity and willingness to tackle daunting scientific questions, and where a good idea is valued and rewarded. Fellows are encouraged to become proficient in the use of state-of-the-art molecular approaches and strive for technical excellence. Thus, for the most part we generate genetically altered mouse strains and primary cell types and develop novel techniques or protocols that we use to (i) identify autoreactive memory T cells that fuel the vicious cycles of remitting and recurrent inflammation that characterizes CNS autoimmune diseases; (ii) identify critical pathways used by pathogenic lymphocytes; and (iii) isolate and characterized various Breg subsets.



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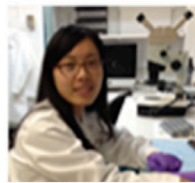
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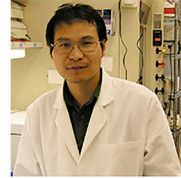
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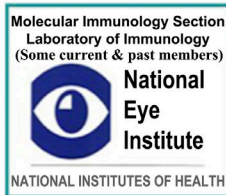
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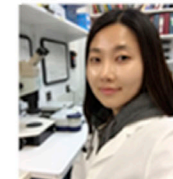
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Rashid M. Mahdi
(Biologist)

Molecular Immunology Section, National Eye Institute, National Institutes of Health (2007–2017).

What did you learn during your PhD and postdoc that helped prepare you for being a group leader?

Success in my positions as a Public Health Service commissioned officer, tenured NIH senior investigator, and chief of the Molecular Immunology Section was made possible by the multidisciplinary education and training I received in graduate school. Joint matriculation at Yale Medical School and Yale Graduate School allowed me to acquire in-depth knowledge of microanatomy, physiology, cell biology, pathophysiology (at the medical school) and epidemiology, immunology, microbiology (virology, parasitology), public health, and biostatistics (at the graduate school). My current position as leader of a medical research team requires a holistic understanding of disease and training in these foundational biomedical disciplines has been an asset to our translational research goals and endeavors.

What were you unprepared for?

Because I had extensive training in immunology, cell biology, biochemistry, and molecular biology, I was offered the opportunity to start my own laboratory after less than 1 yr of postdoctoral training. In retrospect, I am not sure whether that wonderful opportunity

did not stunt my full development as a scientist.

What has been the biggest challenge in your career so far?

The biggest challenge in my career was being a single parent and raising my then 3-yr-old daughter while a third-year grad student and postdoc. Luckily, I later remarried to a wonderful physician-scientist who was also on tenure track at NIH, and we both raised our then precocious 14-yr-old during that tumultuous period in the life of a teenage girl.

What is the best advice you have been given?

With a degree in infectious disease epidemiology, microbiology, and immunology, the logical career track was a postgraduate training at the Epidemic Intelligence Service, Centers for Disease Control. I am indebted to two of my Yale professors whom I admired and considered as mentors, George Palade, 1974 Nobel Prize in Physiology and Medicine winner, and the eminent immunologist, Charles Janeway. They gave me the most impactful career advices. They remarked on my excellent training in molecular cell biology and immunology, and surprisingly, both advised me to go to the

NIH for postdoctoral training in immunology or neuroscience before deciding on whether to pursue a career in epidemiology and tropical diseases.

What hobbies do you have?

I love soccer and tennis. In my youth, I was an excellent soccer player and was good enough to aspire playing for the Cameroon Olympic Soccer Team. However, my mother, a very opinionated and strong-willed woman, was adamant in her belief that all African footballers become drunkards by the

age of 30. The next best thing for me was academia.

Any tips for a successful research career?

An adage in sports is that for a gifted athlete to achieve his/her fullest potential, he/she must be coachable. This also holds true in science. While senior scientists and physician-scientists are committed to training interns and postdoctoral fellows, humility and forbearance is essential for a mutually rewarding research environment for

teaching and learning. Thus, a key to a successful career in science is to “go with the flow” and not to be overly sensitive to constructive criticism.

References

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