DUNCAN STEELE

NIAID LABORATORY AT NIH TO CONDUCT POST-DOCTORAL RESEARCH WHICH WOULD CONTRIBUTE TO THE ROTAVIRUS VACCINE DEVELOPMENT PROGRAMMES CURRENTLY UNDERWAY

JAMES GEAR FELLOW: 1990

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I was awarded the James Gear International Fellowship in 1990 which enabled me to return to the laboratory of Dr Albert Kapikian, Head, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes, Bethesda MD from 1990 to 1992.

I was initially able to visit LID in 1989 for 6 weeks, by invitation from Dr Kapikian, with a PRF travel grant to verify some results from my doctoral research describing the virulence of a specific rotavirus genotype (VP4 P[6]) in African infants. A similar strain with VP4 P[6] was being developed by LID as a vaccine candidate for rotavirus and had just entered Phase 1 studies. Drs Kapikian and Jorge Flores invited me to return to the LID for a post-doctoral period which was only made possible by the James Gear Fellowship.

I spent two years in Bethesda working with Dr Flores on the characterization of the two outer capsid proteins, VP7 and VP4, which elicit the production of neutralizing antibodies in the host and have been the target of all rotavirus vaccine candidates in development, including those licensed and now introduced into routine immunization schedules globally. This technical molecular research in Dr Flores' lab led to the identification of PCR primer cocktails for the targeted genotyping of rotavirus strains by the VP4 and VP7 encoding genes and enabled the rapid dissemination of these techniques to laboratories in Africa and Asia for characterizing rotavirus strains. These techniques, although somewhat refined, are still being used today to describe the diversity of rotavirus strains pre- and post-rotavirus vaccine introduction to assess the vaccine-induced evolution of novel and new emerging rotavirus strains.

In addition, I worked with Dr Kapikian on the immuno-assay assessment of the Rhesus-human reassortant vaccine candidate undergoing clinical evaluation in Venezuelan infants and the characterization of rotavirus strains captured in this Phase 2b efficacy study. This gave me an interesting experience in learning about clinical studies as well as laboratory techniques and opened new horizons.

Besides the obvious benefit of working with the world's leading rotavirus researchers at NIAID and establishing strong personal connections with scientists both inside NIAID and in the USA (eg. Roger Glass, CDC, Harry Greenberg, Stanford University, Dick Ward, CCHMC and others) and globally. The post-doctoral research, made possible by the James Gear Fellowship, firmly established my future career and advanced the opportunity for the development of a "centre of excellence" rotavirus laboratory in South Africa which soon expanded rotavirus research into Africa.

First, the research work that I conducted in Dr Flores' lab led to a regional research agenda resulting in an SA MRC Research Unit in 1996 at the, then, Medical University of Southern Africa (MEDUNSA, now the Sefako Makgatho Health Sciences University). This SA MRC Research Unit was the first fully autonomous research unit funded at an "historically disadvantaged university" and was based on rotavirus research focused on understanding the molecular epidemiology and characterization of rotavirus strains across the continent. As the SA MRC *Diarrhoeal Pathogens Research Unit* became more recognized internationally, the lab recruited strong regional collaboration and the recruitment of post-doctoral fellows and postgraduate students from South Africa and several countries in Africa.

The African Rotavirus Network, now funded by WHO and Gavi, The Vaccine Alliance, was built on this early network and remains a robust research community to this day. Researchers trained at the SA MRC *Diarrhoeal Pathogens Research Unit* have gone on to leadership positions both regionally and globally and many have become stalwart members of an internationally recognized rotavirus community, attaining positions of leadership at WHO and AFRO, the US CDC and many independent academic research teams.

Secondly, the research work that I conducted with Dr Kapikian on the rotavirus vaccine trial, resulted in an invitation from the WHO to conduct a small safety and immunogenicity study of another reassortant rotavirus vaccine developed at NIAID in an African infant population in 1998. We built a vaccine trial centre at MEDUNSA and established a vaccine team with community health care workers, nurses, vaccinators and pharmacists and recruited and trained clinical trial physicians. This small study led to a personal burgeoning interest in, and opportunity for, conducting and coordinating larger Phase 2 and Phase 3 clinical studies with multiple rotavirus vaccines. Between 1998 to 2003, I was tasked with conducting clinical studies with rotavirus and influenza vaccine candidates from Wyeth Vaccines and from GSK Biologicals, as well as WHO.

In 2002, Gavi, The Vaccine Alliance created the Rotavirus ADIP (Accelerated Development and Introduction Program) based at PATH with collaboration between the US CDC and WHO. I was recruited by WHO to be the Focal Point and WHO lead for this partnership with $45M for the evaluation of a global rotavirus agenda. From 2003 at WHO, I coordinated the large multi-country Phase 3 safety and efficacy studies of rotavirus vaccines from GSK Biologicals in Malawi, South Africa and Bangladesh; and from Merck Vaccines in Kenya, Mali and The Gambia and in Bangladesh and Vietnam. In addition, working with CDC colleagues from my postdoc research at NIAID, we established regional networks for rotavirus surveillance and disease burden in all regions. In Africa, this was based on the fledging network set up in 1998 by the SA MRC *Diarrhoeal Pathogens Research Unit*.

PATH, a global non-profit for health, was awarded a large research grant by the Bill & Melinda Gates Foundation to develop alternative safe and efficacious rotavirus vaccines with Indian manufacturers to ensure a global supply of vaccine and to provide low-cost, affordable rotavirus vaccines for the Gavi market. In 2008, PATH offered me the opportunity to support the clinical development of two rotavirus vaccines now licensed as Rotavac, Bharat Biotech, Hyderabad and RotaSIIL, Serum Institute of India, Pune. These vaccines are being used in India and introduced globally including into several countries in Africa. This led to an offer to join the Bil & Melinda Gates Foundation in 2012 to lead and coordinate their strategic investment in enteric vaccines including and beyond rotavirus.

The James Gear International Fellowship provided me the opportunity to develop an established research career in rotavirus and in rotavirus vaccine research. The connections that I made at NIAID have remained effective and durable partnerships and collaborations which have continued to propel me into advanced positions at the WHO in 2003, PATH in 2008 and to the Bill & Melinda Gates Foundation in 2012. It is illuminating to think how my career path could have borne fruit and unfolded without the opportunities that the James Gear Fellowship initially presented me in 1990-1992.

I have a great deal to be grateful for in my career. The James Gear Fellowship is an essential anchor in my lifelong research into rotaviruses and the vaccines that are now being used daily and with increasing impact globally. However, the benefits I am exceedingly grateful for extend beyond the opportunity that the Fellowship afforded me to the mentorship and friendships that I gained both regionally and globally. The Fellowship was the launching pad to a network of collaborators and research and to the possibilities of a new generation of young, enthusiastic African researchers.