NIH Director's Award Recognizes Rapid Response to Avert Potential Health Crisis

By Stuart Le Grice, Guest Writer, and Nancy Parrish, Staff Writer

In July 2012, members of a multidisciplinary research team of both SAIC-Frederick and NCI Center for Cancer Research scientists were recognized with the NIH Director's Award for their outstanding work to rapidly evaluate a potential threat to the nation's blood supply.

The IRP XMRV Working Group, from left: Vineet KewalRamani, Ph.D., head, Model Development Section, DRP (NCI); Rachel Bagni, Ph.D., Molecular Detection and Viral Technology, PEL (SAIC-Frederick); Jeffrey Lifson, M.D., director, ACVP (SAIC-Frederick); Alan Rein, Ph.D., head, Retrovirus Assembly Section, DRP (NCI); James Hartley, Ph.D., head, Technology Development, PEL (SAIC-Frederick); Mary Kearney, Ph.D., head, Translational Research, DRP (NCI); and Stuart Le Grice, Ph.D., head, RT Biochemistry Section, DRP (NCI).

Known as the XMRV Working Group, the researchers came together in response to findings presented at the May 2009 Cold Spring Harbor Retroviruses Meeting that xenotropic murine leukemia virus-related virus, or XMRV, might be present in approximately 3 percent of the U.S. population, raising both public health issues and concern for contamination of the nation's blood supply. XMRV was believed to have a potential link to prostate cancer and chronic fatigue syndrome (see article on page 4).

The findings prompted the NCI Intramural Research Program (IRP) to immediately form the XMRV Working Group to develop, implement, and make available diagnostic reagents for rapid, accurate, and reliable detection of the presence of XMRV in human blood.

The group, comprising scientists from both SAIC-Frederick and NCI, developed an action plan, and by December 2009, the Protein Expression Laboratory reported successful construction and subsequent purification of 40 recombinant clones expressing all XMRV antigens. These clones, then, could function as immunological reagents that would be used to diagnose the presence of XMRV antibodies in patient samples.

Importantly, these reagents were also made available (through the NIH AIDS Reagent Program) to the extramural community to accelerate XMRV research and allow sharing of a common set of reagents.

NCI–SAIC-Frederick Collaboration Ensured Success

At the same time, researchers in the HIV Drug Resistance Program (DRP) developed an assay to detect and quantify XMRV DNA (from tissue) and RNA (from plasma). "This assay would be used, in part, to standardize the method of detection when multiple laboratories might be involved in diagnosis," said Stuart Le Grice, Ph.D., head, Reverse Transcriptase (RT) Biochemistry Section, DRP, who led the XMRV Working Group. Since ultrasensitive XMRV nucleic acid (DNA and RNA) detection methods were not available, DRP researchers developed and standardized the detection methods.

In addition, the Molecular Detection and Viral Technology group developed and standardized the immunological reagents, which required natural viral antigens. In response to this need, the large-scale virus culture facilities of the AIDS and Cancer Virus Program (ACVP) were recruited to produce XMRV. Finally, the DRP researchers developed an assay using the DERSE indicator cell line, which reduced the time needed to detect low levels of replicating XMRV in cell culture from months to a matter of weeks.

"Effective Efforts to Protect Public Health"

The NIH Director's Award recognized the XMRV Working Group's "exceptionally rapid and effective efforts to protect public health in response to a potential widespread viral threat." Although subsequent studies revealed that XMRV does not pose a threat to public health, "this dedicated group of IRP scientists demonstrated an ability to assemble a multidisciplinary team to prepare, standardize, and make available reagents for diagnostic virology," Le Grice said. Reagents were prepared with existing manpower and resources, and without interrupting the normal productivity of each group involved, and the project was completed within a 12-month period.

Le Grice describes the award as recognition of "not only the depth of retrovirology expertise within the National Cancer Institute, but also the ability of the IRP to rapidly re-focus its considerable resources in response to an emerging public health issue." ■

Stuart Le Grice is head, Reverse Transcriptase (RT) Biochemistry Section, HIV Drug Resistance Program.