

Veterinary college's research team contributes to landmark heparin study

By Jeffrey Douglas, APR
(540) 231-7911, jdouglas@vt.edu

BLACKSBURG, VA., April 29, 2008 -- Researchers in the Virginia-Maryland Regional College of Veterinary Medicine at Virginia Tech have provided critical support for an international research effort led by the Massachusetts Institute of Technology that is helping resolve the global public health threat caused by contaminated heparin.

Heparin, a blood thinner commonly used in kidney dialysis and heart surgery, has been linked to allergic reactions, hypotension and other medical disorders that have led to 81 deaths in the United States and Germany so far.

Government officials and scientists from countries around the world have been working since January 2008 to learn more about mysterious adverse patient reactions associated with heparin. United States Food and Drug Administration officials believe the contaminant originated from Chinese factories that manufacture the drug for Baxter International.

The Massachusetts Institute of Technology-led multi-institutional study, which was recently published in the *New England Journal of Medicine* and *Nature Biotechnology*, has demonstrated a biologic linkage between the suspected contaminant -- over-sulfated chondroitin sulfate, otherwise known as OSCS -- and the onset of clinical disease. Establishing this relationship will play an important role in helping authorities determine the safety of the global heparin supply and help prevent the deadly problem from occurring again.

The story of the veterinary college's role in the multi-center research effort is an example of the unexpected opportunities that can arise from routine scientific inquiry and academic collegiality. It also speaks to the dedication and agility of a team of Virginia Tech researchers, administrators, and technical personnel who were able to design and obtain approval for the project, assemble the needed resources, and perform and complete the critically needed scientific experiments within a short time period.

Existing research conducted by Dr. Ram Sasisekharan and colleagues at the Massachusetts Institute of Technology had established that the over-sulfated chondroitin sulfate contaminant was responsible for the clinical problems that were being observed in humans. But, the biological link for proving that it induced the adverse events was needed for further validation. Sasisekharan's team at the institute had *in vitro* data to indicate that the contact system was activated in plasma from pigs when exposed to the contaminant or contaminated heparin. The Food and Drug Administration wanted animal modeling work conducted for further validation.

Dr. Elankumaran Subbiah, a virologist and assistant professor in the Virginia-Maryland Regional College of Veterinary Medicine's Department of Biomedical Sciences and Pathobiology, had an existing collaboration with Sasisekharan at the institute on influenza A viruses. Faced with the urgent Food and Drug Administration request for rapid animal modeling work, Sasisekharan contacted Subbiah to see if the veterinary college could conduct the critical animal modeling work on an extremely fast timeframe.

Subbiah immediately contacted Dr. Nammalwar "Nathan" Sriranganathan, a professor in the same department and senior researcher in the Center for Molecular Medicine and Infectious Diseases; Dr. Kevin Pelzer, an associate professor in the Department of Large Animal Clinical Sciences joined the team. Sriranganathan set the ball rolling by contacting all the administrative links and assembled all the resources necessary for the task.

Facing a daunting task but understanding the urgency of the global public health problem at hand, the team decided to proceed. Working feverishly into the night, the group established a study design and had it approved by the Virginia Tech's Institutional Animal Care and

Use Committee within nine hours. This would not have been possible without the cooperation of the Institutional Animal Care and Use Committee team, and Associate Vice Provost for Research Compliance David Moore, who signed off on the project at 2 a.m. from India.

The team then worked with Dr. Cynthia Wood in Virginia Tech's College of Agriculture and Life Sciences and was able to procure the research animals. Thus began an arduous, two-week, 24/7 marathon process that ultimately concluded that the contaminant might in fact activate the suspected pathways in pigs, just as they were believed to do in people, mimicking the adverse events reported. The work played a pivotal role in validating the Massachusetts Institute of Technology hypothesis. Additional experiments are being planned at the veterinary college to determine the dose response as well as effects of routes of administration to confirm our findings.

"Every single star aligned properly to get this done," said Subbiah, adding that the work could have never been accomplished without the support and collaboration from many different sectors of the Virginia Tech research community, from the Institutional Animal Care and Use Committee team to members of the veterinary college's administration to Veterinary Teaching Hospital Director Dr. William Pierson and anesthesiologist Dr. Cindy Hatfield to the swine facility.

Project team members included Subbiah, Sriranganathan, Pelzer, and graduate student Thomas Rogers-Cotrone. Key assistance was also provided by Teaching and Research Animal Care Support Services members Pete Jobst and Andrea Aman, according to Subbiah.

The result of this landmark study is published in the New England Journal of Medicine as an advanced online publication on April 23, 2008. [The article is available online.](#)

##08299##

Invent the Future

Virginia Polytechnic Institute and State University
An equal opportunity, affirmative action institution