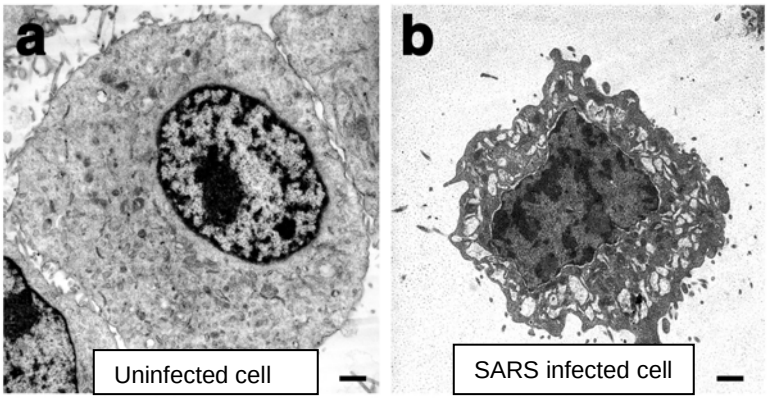
Eric Freundt …virologist deciphering SARS

"Through the NIH-Oxford program, I have been able to collaborate with leading virologists at the NIH and at Oxford…. I had the opportunity to travel to China to meet with scientists with expertise in SARS during the initial phases of my research. While in China we were shown samples from SARS patients that exhibited similar features to what we had observed while working with the virus in model cell lines. This convinced us that our research would likely relate to the disease in humans which was a great experience I never would have had in an ordinary graduate program."

Beijing, China

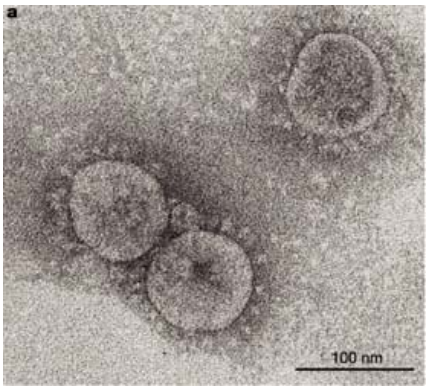
Eric Freundt was raised in Tennessee and attended Middle Tennessee State University where he graduated Summa Cum Laude from the Honors College with a B.S. in Biology and Chemistry in 2003. As an undergraduate he had a passion for virology and undertook an honors research project which led to the discovery of a novel tick-borne enterovirus in patient cerebral spinal fluid. So it was natural for Eric to pursue a virology project in his graduate work as the basis for a future career in research of host-pathogen relationships in emerging infections. He entered the NIH-Oxford program because of the wealth of opportunities in infectious disease research with a choice of over 200 different

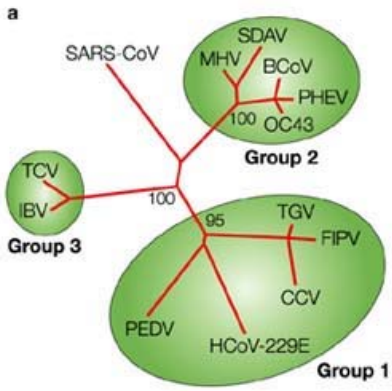
laboratories encompassing all of the major microbial pathogens. He chose a collaborative project with Xiaoning Xu at the Weatherall Institute for Molecular Medicine at Oxford and Dr. Michael Lenardo at the National Institute for Allergy and Infectious Diseases at NIH. Eric's work addressed the question of why the SARS-CoV virus causes lethal pathology in humans whereas the other human



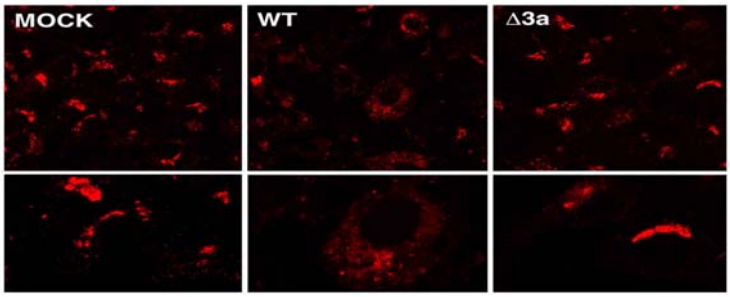
coronaviruses cause only the equivalent of the common cold. Since the nucleotide coding sequence of SARS virus was the fastest to be unraveled for any virus in history, Eric could look directly into the genes of the virus to get clues to this mystery. He found that there were 10 small unique genes encoded in the SARS-CoV virus and he set about to test them, one-by-one, for their ability to damage cells and potentially account for the pathogenesis of SARS. He found that one gene, termed 3A, had a striking ability to kill any cell in which it was expressed. Since cell death was one of the primary features observed in diseased tissue in SARS patients, this was a major insight. He then began to examine the molecular basis of 3A lethality. He found that it caused a previously unrecognized toxic effect on the Golgi apparatus – an organelle essential for the final processing of newly produced proteins. The 3A protein caused a fragmentation and disintegration of the Golgi leading to the demise of the cell. He also found that this novel form of cytopathicity was also induced by other viruses including certain viruses in the smallpox family.

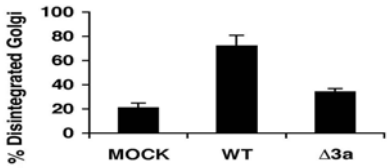
Xiaoning Xu, Michael Lenardo, Dr. Wei, Minister of Health for Beijing City during the SARS epidemic, and Eric Freundt at a dinner in Beijing, China, 2003.





SARS-CoV, a coronavirus, which is so-named because of the "crown-like appearance of the surface coat protein on the virus particles, visualized by electron microscopy. The nucleotide sequence of the SARS virus shows it to be distantly related to other coronaviruses.





"As an undergraduate, I had the opportunity to work with Dr. Stephen Wright on a novel mode of transmission of human enteroviruses. This research led me to become interested in viral pathogenesis or how viruses disrupt normal cellular processes and cause disease. When I entered the NIH-Oxford partnership program, the severe acute respiratory syndrome coronavirus (SARS-CoV) had just emerged and posed important research questions. I chose to focus on understanding the functions of novel SARS-CoV proteins. My graduate work has elucidated the mechanism by which the SARS-CoV causes cell death and leads to fatal lung damage in its victims. Our collaboration has uncovered a protein unique to the SARS coronavirus which contributes to the ability of the virus to kill cells during infection by a novel mechanism of Golgi fragmentation."

Eric Freundt