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RESEARCHERS TRACE CORONAVIRUS OUTBREAK IN CHINA TO SNAKES

22 JANUARY 2020 - Emerging viral infections—from bird flu to Ebola to Zika infections—pose major threats to global public health, and understanding their origins can help investigators design defensive strategies against future outbreaks. A new study provides important insights on the potential origins of the most recent outbreak of viral pneumonia in China, which started in the middle of December and now is spreading to Hong Kong, Singapore, Thailand, and Japan. The findings are published early online in the Journal of Medical Virology.

The study notes that patients who became infected with the virus—which is a type of virus called a coronavirus and was named 2019-nCoV by the World Health Organization—were exposed to wildlife animals at a wholesale market, where seafood, poultry, snake, bats, and farm animals were sold.

By conducting a detailed genetic analysis of the virus and comparing it with available genetic information on different viruses from various geographic locations and host species, the investigators concluded that the 2019-nCoV appears to be a virus that formed from a combination of a coronavirus found in bats and another coronavirus of unknown origin. The resulting virus developed a mix or "recombination" of a viral protein that recognizes and binds to receptors on host cells. Such recognition is key to allowing viruses to enter host cells, which can lead to infection and disease.

Finally, the team uncovered evidence that the 2019-nCoV likely resided in snakes before being transmitted to humans. Recombination within the viral receptor-binding protein may have allowed for cross-species transmission from snake to humans.

"Results derived from our evolutionary analysis suggest for the first time that snake is the most probable wildlife animal reservoir for the 2019-nCoV," the authors wrote. "New information obtained from our evolutionary analysis is highly significant for effective control of the outbreak caused by the 2019-nCoV-induced pneumonia."

An accompanying editorial notes that although the ultimate control of emerging viral infections requires the discovery and development of effective vaccines and/or antiviral drugs, currently licensed antiviral drugs should be tested against the 2019-nCoV.

Full citation: *"Homologous recombination within the spike glycoprotein of the newly identified coronavirus may boost cross-species transmission from snake to human." Wei Ji, Wei Wang, Xiaofang Zhao, Junjie Zai, and Xingguang*

Li. Journal of Medical Virology; Published Online: January 22, 2020, DOI: 10.1002/jmv.25682. URL Upon Publication: https://onlinelibrary.wiley.com/doi/10.1002/jmv.25682

TAKING AIM AT GASTRIC CANCER: NEW APPROACH TO SELECTIVE CHEMOTHERAPY

23 JANUARY 2020 - A novel drug, named "FerriIridium", can simultaneously help diagnose and treat gastric cancer. The initially weakly active precursor (prodrug), based on an iridium-containing compound, is selectively activated only after reaching the interior of a tumor cell. This is possible because of the higher amount of iron present there, report scientists in the journal Angewandte Chemie. Selective activation reduces undesired side effects.

Cells transport substances from their exterior to their interior by folding in small regions of their membrane and then binding them off (endocytosis). This is how FerriIridium enters target cells. The resulting vesicles then fuse with lysosomes. These cell organelles have an acidic environment that contains trivalent iron ions, Fe(III), and enzymes, with which they dismantle cell components that are no longer needed. In gastric cancer cells, the Fe(III) concentration within the lysosomes is significantly elevated.

Scientists working with Yu Chen and Hui Chao at Sun Yat-Sen University, Guangzhou, and Hunan University of Science and Technology, Xiangtan (China) made use of this feature. They equipped FerriIridium with a special functional group (the m-iminocatechol group) that selectively binds to Fe(III). When bound, the functional group is oxidized while the iron ions are reduced to Fe(II). Under the acidic conditions within the lysosomes, the FerriIridium is then split into two components: an iridium complex and a benzoquinone derivative.

This reaction mechanism has a threefold effect. First, Fe(II) ions can catalyze a reaction that produces highly reactive hydroxyl radicals. Second, benzoquinones are highly oxidizing. With certain cellular substances, such as NADPH, they form hydroxyquinones, which react with oxygen to produce radical oxygen species, as well as hydrogen peroxide, which in turn can react with Fe(II) to produce hydroxyl radicals. Benzoquinone compounds can also disrupt cellular respiration. The radicals destroy the lysosomes, releasing their contents. Third, the splitting of FerriIridium drastically increases both the phosphorescence and the toxicity of the iridium complex. The phosphorescence can be used to diagnose the tumor. Most importantly, however, the toxic iridium complex is absorbed by mitochondria, the "cellular power plants". It destroys them from the inside out by collapsing their membrane potential. Together, these effects lead to the death of the gastric cancer cells and shrinking of the tumors, as demonstrated by experiments on cell lines and mice.

Full citation: *"Ferrildium: a lysosome-targeting iron(III)- activated iridium(III) prodrug for chemotherapy in gastric cancer cells." Hui Chao, Shi Kuang, Xinxing Liao, Xianrui Zhang, Thomas Rees, Ruilin Guan, Kai Xiong, Yu Chen, Liangnian Ji. Angewandte Chemie International Edition; Published Online: December 11, 2019, DOI: 10.1002/anie.201915828 URL Upon Publication: https://onlinelibrary.wiley.com/doi/abs/10.1002/anie.201915828*