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NRC Institute for Biological Sciences

Engineered Biosynthetic Pathway for Sialic Acid Analogs and its Use for the Development of Anti-Infectives

The Business Opportunity

There is clearly an unmet need for anti-influenza drugs that are more effective than those currently available, and ideally that are effective against various strains of influenza and that are not prone to the development of resistance. The unique features of the NRC-IBS technology, with its anticipated efficacy against numerous strains, possibly including avian flu, will enable it to compete effectively against such products. We also note that the market is quite large, and is likely to continue to grow over the coming years. The technology may also result in the development of agents against other viral infections, and against bacterial infections.

According to the U.S. Centers for Disease Control, "While getting a flu vaccine each year is the first and most important step in protecting against flu, antiviral drugs are a second line of defense in the prevention and treatment of flu."1.

Influenza is a common respiratory infection in humans characterized by fever, cough and severe muscle pain. Influenza A, a member of the Orthomyxoviridae family of RNA viruses, has been responsible for all flu pandemics documented and is known to infect humans, other mammals and birds (avian influenza). In humans, it is the most virulent influenza virus causing most influenza-associated disease. Influenza A viruses may be further classified based on two viral surface glycoproteins, a hemagglutinin (H) and a neuraminidase (N) or sialidase. 16H and 9N subtypes have been identified so far, all of which are found in birds. Only the H1, H2, H3, N1 and N2 subtypes are known to commonly infect humans, but human pandemic strains may emerge from avian viruses, such as the recent threat of avian H5N1.

The Technology

NRC-IBS technology comprises novel compounds, naturally occurring bacterial sialic acid analogs2,3, which potentially may inhibit sialidase/sialidase-like enzymes. This technology not only allows for the efficient production of these sialidase inhibitors, but it may also be harnessed for engineering a family of natural and unnatural derivatives. These derivatives could then be used in a 'cocktail' approach further preventing the development of therapeutic resistance. These compounds represent potential therapeutic agents for use against influenza and potentially against other viral/bacterial infections (for example, against P. aeruginosa infections associated with cystic fibrosis). It is thought that these compounds may be naturally produced by bacteria to combat viruses within the avian gastrointestinal tract. Since influenza sialidases associated with human illness are also found in birds, it is therefore reasonable to postulate that these compounds could be well-tolerated by human subjects. Also, these natural compounds share similarity with anti-influenza compounds already in the marketplace, further precedence for their non-toxicity in humans. As there currently are no products that are entirely ("100%") effective in the prevention and/or treatment of the flu, a novel anti-influenza agent that provides a greater scope of protection would certainly seem to address an unmet need.

Patent Position

Patents Pending – NRC IBS case 12036

Key Publications

1 "Antiviral Drugs General Information", U.S. Centers for Disease Control and Prevention website, (http://www.cdc.gov/flu/about/qa/antiviral.htm)

[2] Schoenhofen, I.C., McNally, D.J., Brisson, J-R., and Logan, S.M. (2006) Elucidation of the CMP-pseudaminic acid pathway in *Helicobacter pylori*: synthesis from UDP-*N*-acetylglucosamine by a single enzymatic reaction. *Glycobiology* 16: 8C-14C.

[3] Schoenhofen, I.C., Vinogradov, E., Whitfield, D.M., Brisson, J-R., and Logan, S.M. (2009) The CMP-legionaminic acid pathway in Campylobacter: biosynthesis involving novel GDP-linked precursors. Glycobiology, epub ahead of print.

The Market

In the U.S., an estimated 25–50 million cases of the flu are currently reported each year — leading to 150,000 hospitalizations and 30,000–40,000 deaths yearly. If these figures were to be estimated incorporating the rest of the world, there would be an average of approximately 1 billion cases of flu, around 3–5 million cases of severe illness, and 300,000–500,000 deaths annually." (FluFacts.com) According to the World Health Organization, "Influenza rapidly spreads around the world in seasonal epidemics and imposes a considerable economic burden in the form of hospital and other health care costs and lost productivity. In annual influenza epidemics 5-15% of the population are affected with upper respiratory tract infections. Hospitalization and deaths mainly occur in high-risk groups (elderly, chronically ill)." Throughout history, a pandemic has occurred every 10-40 years, infecting a large proportion of the world's population, each resulting in the deaths of at least a million people.

Technology Transfer Possibilities

- A commercial exploitation license for the technology.
- Development of this technology through a joint collaboration.

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