Extended Abstract Journal of Clinical Developmental Biology 2017
Vol.2 No.2

Infectious Diseases 2017: New antiviral molecules from *Phyllocaulis boraceiensis* mucus

Ana Rita de Toledo Piza[1, 2]

[1] Limace Biotecnologia, Brazil,
[2] University of São Paulo, Brazil

Influenza A virus belongs to the family *Orthomyxoviridae* and cause severe health conditions, often leading to pneumonia. The influenza viral genome consists of negative-sense RNA (vRNA) packaged in viral ribonucleoprotein (vRNP) complexes. This enveloped virus, contains eight genomic segments that encode up to 13 proteins, such as, hemagglutinin (HA), neuraminidase (NA), matrix 1 (M1), matrix 2 (M2), nucleoprotein (NP), non-structural protein 1 (NSP1), non-structural protein 2 (NS2; also known as nuclear export protein, NEP), polymerase acidic protein (PA), polymerase basic protein 1 (PB1), polymerase basic protein 2 (PB2) and polymerase basic protein 1-F2 (PB1-F2). The viral envelope formed by a lipid bilayer contains the viral transmembrane proteins: HA, NA, and M2. This virus possess a number of mechanisms that enable it to invade host cells and subvert the host cell machinery in the many steps of their life cycle. The World Health Organization (WHO), through the Global Influenza Monitor keeps track of the activity of the disease caused by influenza virus worldwide. Currently, there are three types of influenza viruses, A, B and C, based on the antigenic and genetic differences of the inner proteins and genome structure. Influenza Type A virus is categorized into subtypes based on two surface antigens: hemagglutinin and neuraminidase. The subtypes of influenza virus, type A/H1N1, type A/H3N2 and type B, infect humans, causing massive and rapidly evolving global epidemics. Recently, it was observed that patients infected with the pandemic H1N1 (pdmH1N1) virus developed severe disease and consequently died, while those infected with seasonal influenza virus did not develop severe diseases. The severe “Spanish flu” in 1918, caused by the H1N1 strain, was the worst pandemic in recorded history and resulted in approximately 50 million deaths worldwide. During the year 2009, 214 countries reported cases of H1N1 pandemic influenza with more than 18,000 deaths. Influenza A (H1N1) virus remained a great health issue, and there are few treatment options. Vaccination remains the primary method for prevention of influenza. However, vaccines only protect against antigenically related strains and exhibited limited efficacy. Antigenic drift, or mutations mainly of the segments encoding the surface proteins and promote evasion of the host immune system. The high diversity of potential emerging zoonotic and pandemic viruses become difficult to select the right strains for vaccine production, and consequently allows a slightly varied virus to re-infect the population. The antiviral drugs approved for the influenza virus prevention and therapy are the viral M2 protein, Amantadine ® (Symmetrel) and Rimantadine ® (Flumadine), or the neuraminidase inhibitors, Zanamivir ® (Relenza) and Oseltamivir Carboxylate ® (Tamiflu). M2 is tetrameric proton channel activated by acidic pH, which is important for genome unpacking during virus entry. The M2 channel transports protons from the vacuolar space into the interior of the virion, while Neuraminidase inhibitors act as a competitive inhibitor of the activity of the viral neuraminidase enzyme. The M2 ion-channel inhibitors is effective only against type A viruses (Pielak and Chou 2010), while the neuraminidase inhibitors, is effective against both type A and B viruses. Depending on the way, as was detected, the levels of antiviral resistance are classified as genotypic, phenotypic and clinical resistance. These antiviral drugs facing drug resistance in new strains. Oseltamivir and Zanamivir are the two main neuraminidase inhibitors used for the treatment of Influenza. The clinical use of neuraminidase inhibitor oseltamivir increased substantially during the recent H1N1 pandemic. Oseltamivir resistance was identified in non-pandemic influenza viruses, as well as H1N1 pandemic influenza A viruses. The most common mutation associated with oseltamivir resistance is the amino acid change H275Y in the neuraminidase (NA) protein. Among 2007–2008, the oseltamivir-resistant strain of the seasonal H1N1 virus was efficiently transmitted, causing a widespread epidemic of drug-resistant influenza. Molluscan species biosynthesized secondary metabolites that are crucial constituents for its defenses against viruses. The secondary metabolites are extracted from the innate immune system, which is provided by physical barriers, such as, shell, skin, mucus, and epithelium. These exudates exhibited a variety of immune mechanisms that include antiviral compounds that exhibit diverse mechanisms of action against a wide variety of viruses, including many that are human pathogens. Several bioactive molecules extracted from mollusks exhibited potential pharmaceutical or industrial applications. Besides, this can be used as a source of antibacterial and antiviral drugs. However, most members of the phylum Mollusca have not studied for the search of bioactive compounds. The exudate extracted of marine mollusks from the family *Muricidae* are used in traditional medicines for thousands of years. The brominated indoles extracted exhibited anti-inflammatory, anti-cancer and steroidogenic activity, while the choline esters showed muscle-relaxing- and pain relieving properties.

Terrestrial gastropods exude mucus by the body surface, when traveling, to protect its body from mechanical injury, desiccation or contact with harmful substances. Mucus of mollusks has been studied as a source of new natural compounds with diverse biological activities as its capability of inducing proliferation and

This work is partly presented at Joint Event on International Pediatrics, Infectious Diseases and Healthcare Conference & 8th International Conference on Bacteriology and Infectious Diseases 2017.

remodeling tissue and their antiviral capacity. Fungus and viruses are related to a range of infectious diseases in humans and animals. Viruses cause worldwide outbreaks and pandemics in humans and animals every year with considerable morbidity and mortality. The molecular diversity of secondary metabolites extracted from mollusks is a good alternative for the discovery of novel bioactive compounds with unique structures and diverse biological activities. *Phyllocaulis boraceiensis* is a hermaphroditic slug that exudes mucus, in which was detected some molecules that exhibited potent antiviral activity against Measles, Influenza, Herpes, Rubella and Zika virus. In order to identify, isolate, purify and sequence molecules present in the mucus of the land slug *P. boraceiensis* with antiviral action "in vitro" were used fragmentation by chromatography and mass spectrometry in order to determine the active molecules and assay of biological activity, qPCR and immunofluorescence labeling to determine the biological activity.

This work is partly presented at Joint Event on International Pediatrics, Infectious Diseases and Healthcare Conference & 8th International Conference on Bacteriology and Infectious Diseases 2017.