The same effect observed in cancer cells is detected in disease caused by pige

UFRGS research group identifies metabolic behavior that can assist in the diagnosis of cryptococcosis

First published -January 10, 2020 - by Mariana Bier

Researchers from the Faculty of Pharmaceutical Sciences and Hospital de Clínicas from the Federal University of Rio Grande do Sul (UFRGS) conducted a study that suggests new perspectives to characterize the behavior of the carrier of cryptococcosis, also known as "pigeon disease". In humans, this pathology reaches the pulmonary and brain pathways, which can trigger pneumonia and meningitis in those who are infected. Initially, however, the disease does not appear as aggressively as most infections, what makes diagnosis difficult.

Pigeons are hosts of the fungi that cause cryptococcosis - Photo: Rochele Zandavalli / UFRGS - Archive

Cryptococcosis is caused by fungi *Cryptococcus neoformans* and *Cryptococcus gattii*, which are found in tree bark, as well as in bat and pigeon droppings – that is why it is considered a pigeon disease. Pigeons are not affected by this pathology, as they are only hosts of the fungi. The problem is when the fungi pass through the animals' digestive tract and leave through the feces. It is in contact with excrement, including through air, that human beings can be contaminated. This is one of the reasons for the high incidence rate of this disease in metropolises.

The researchers concluded, through experiments, that cryptococcosis has a behavior called the "Warburg effect", the same observed in cancer cells that causes them to alter the metabolism to support the accelerated growth of the tumor. This information can help both the diagnosis of the disease and future therapies, since there are specific drugs with a focus on the Warburg effect that can be evaluated for cryptococcosis in future experiments, as the researchers at UFRGS intend to find out.

Experiment with living organisms

Scientists experimented with living organisms to identify the pathological condition of the disease, that is, to observe the set of symptoms that are associated with cryptococcosis. They injected the disease fungus into mice to analyze the development of infectious processes in an animal body. Then, they removed the lungs from the rodents to characterize the proteins present in them after infection. Walter O. Beys da Silva, higher education professor at the Faculty of Pharmaceutical Sciences at UFRGS and research member, clarifies that this procedure is important to identify which proteins appeared more and which decreased in the rodent's organism. He explains that, with this type of knowledge, it is possible to think of some strategy to reverse the disease.

The higher education professor also says that knowing the effects of the fungus' action can also be an advance to develop new treatments for this infectious disease in the future. "Now we want to specifically understand which cells are involved in this process and investigate something related to cryptococcosis therapy," he reports. The results of the research so far are important to facilitate the diagnosis of the disease.

Cryptococcosis in relation to AIDS

There is no official data regarding the occurrence of cryptococcosis in Brazil, as it is not considered a compulsory notification disease, that is, it is not a disease that the law requires to be reported to public health authorities. However, one of the most worrying factors of the pathology is that it affects both healthy people – through the *gatti* fungus – and people with low immunity, such as those living with Acquired Immunodeficiency Syndrome (AIDS). When associated with this syndrome, cryptococcosis is one of the main opportunistic infections – those that take advantage of the weakness of the body's defenses. According to the Brazilian Ministry of Health, cryptococcosis infection by the *neoformans* fungus represents the main cause of death in individuals with AIDS.

In relation to Brazilian cities with AIDS detection rates (number of new diagnoses) per 100,000 inhabitants, Porto Alegre is the third capital with the highest rate on the list. Rio Grande do Sul is the second state with the highest detection rate, behind Roraima, according to records from the Ministry of Health's HIV/AIDS 2019 Epidemiological Bulletin. Such references show the importance of studies on cryptococcosis, since the capital of Rio Grande do Sul is one of the cities at risk for the disease due to the number of people living with AIDS in the metropolis.

About the Study

The study was carried out at the Faculty of Pharmaceutical Sciences and at Hospital de Clínicas, in collaboration with researchers from the Center of Biotechnology and Faculty of Veterinary Sciences at UFRGS, in addition to the American research institutes *Sanford Burhan Prebys Medical Discovery Institute* and *Scripps Research*. The research results were recently published in the international scientific journal named *Journal of Proteome Research*.

Scientific Article

Rosa, R. L., Berger, M., Santi, L., Driemeier, D., Barros Terraciano, P., Campos, A. R., & Beys-da-Silva, W. O. (2019). Proteomics of rat lungs infected by Cryptococcus gattii reveals a potential Warburg-like effect. *Journal of Proteome Research*, *18*(11), 3885-3895.

Translated into English by Juliana da Silva de Melo, under the supervision and translation revision of Elizamari R. Becker (P.h.D.) – IL/UFRGS.