ICU
MANAGEMENT & PRACTICE

The Rusty and Sweet Side of Sepsis

Sepis affects approximately 18 million people worldwide per year. This corresponds to 1400 deaths per day. It is estimated that sepsis is the cause behind 135,000 and 215,000 casualties in Europe and the U.S. respectively. Related treatment costs accumulate to €7.6 and €17.4 billion in these regions.

A research team led by Miguel Soares at the Instituto Gulbenkian de Ciência in Portugal have discovered an unsuspected mechanism that is protective against sepsis. The team used experimental models of sepsis in mice and their findings could potentially provide new avenues for therapeutic approaches against sepsis. Study findings are published in the journal Cell.

It's unfortunate that even though sepsis is more common than heart attack and more lethal than cancer, a large majority of people don't even know what it is. Sepsis refers to our body's response to an infection that spreads towards different parts of the body. Our immune system tries to kill the microbes responsible for this systemic infection and sometimes manages to do so but while this happens, the normal functioning of our vital organs such as the brain, heart, liver, kidney or lungs is affected. In severe cases, these organs could stop functioning properly, leading to the patient's death.

The severity of the disease varies in different individuals and so does their response depending on the type of infection, any coexisting illnesses, age and genetic characteristics. It has still remained unclear why some patients are able to control it better while others succumb to it.

According to the Miguel Soares team, individuals that do not succumb to sepsis develop a protective response that maintains the function of their vital organs. Through their experiments, they have discovered which mechanism is vital to develop this disease tolerance to sepsis. These researchers claim that a key element to promote tolerance is based on how the levels of iron are controlled in other tissues. Prior research suggests that the pathogenesis of sepsis is associated with deregulation of glucose metabolism.

The Miguel team found that both these mechanisms are linked. Controlling iron metabolism is necessary to sustain the production of glucose in the liver so that it can be used a source of energy by other organs.

During the study, sepsis was induced in mice and disease progression was compared in mice that expressed ferritin compared to those who did not. It was observed that ferritin is necessary for the liver to produce glucose after an infection and to protect the mice from succumbing to sepsis. Results thus show that ferritin controls glucose production in the liver which in turn maintains glucose levels allowing survival. Without ferritin, the glucose levels will drop and the mice would die from sepsis.

In addition, the team also found why ferritin is regquired for the liver to produce glucose. The process is dependant on a molecular mechansim that controls the the expression of one of the key genes involved in this process, known as glucose 6 phosphatase. When ferritin is absent, iron deregulates Glucose 6 phosphatase and the liver loses its capacity to secrete glucose making it difficult for the vital organs to use it as a source of energy.

The authors thus conclude that iron must be controlled in the liver so that it does not interefere with the production of glucose. This entire process relies on the expression of ferritin.

"This is a great example on how basic research conducted in a multidisciplinary environment such as the one provided by the Instituto Gulbenkian de Ciência, without an immediate commercial interest, can have a global impact on the treatment of a major disease that affects over 18 million individuals per year worldwide. Our mission is to make discoveries so that these can be eventually translated into treatments of major diseases". says Miguel Soares.

Source: **Instituto Gulbenkian de Ciência (IGC)**
Image Credit: Rui Chafes

Published on : Wed, 21 Jun 2017