Portuguese scientists show Schistosoma haematobium direct link to tumours

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Schistosoma haematobium (S. haematobium) is a parasitic flatworm that infects millions of people, mostly in the developing world, and is associated with high incidence of bladder cancer although why is not clear. Now, however, two works by Portuguese researchers just out in The Journal of Experimental Pathology [1] and the International Journal of Parasitology [2] reveal that cells infected in laboratory with S. haematobium, acquire cancer-like characteristics and, when injected into mice develop into tumours.

The research identifies as well the host molecules linked to the carcinogenic changes, suggesting that these could be used as therapeutic targets to prevent bladder cancer. These results help to explain the link between S. haematobium and can be relevant also to other cancer-linked chronic infections, in particular to those linked to infections difficult to treat such as hepatitis C.

Schistosomiasis, also known as snail fever - since part of the parasite life cycle occurs in these animals - is a potential fatal disease that, according to the World Health Organization, infects 200 million people and is endemic in as much as 76 tropical developing countries. The disease, spread through contaminated waters, is only second to malaria in rates of infection and public health impact throughout the developing world, but has been one of many neglected tropical diseases until very recently, when globalization and its associated intense migration flux has brought it into the light. Infection by S. haematobium - a member of this family - is particularly relevant due to its association to bladder cancer. In fact,

while the disease can be treated - in the sense that the parasites are killed -their calcified eggs can remain trapped in the bladder creating a chronic infection that is linked to the appearance of cancer. In fact, in regions where S. haematobium is endemic bladder cancer can be the most common cancer in men and the second in women, just behind breast cancer, accounting for as much as 30% of all cancer cases.

In an attempt to understand this worrying link between infection and cancer Mónica Botelho, José Carlos Machado, José Manuel Correia da Costa and colleagues at the Parasitology lab, National Institute of Health, the Institute of Pathology and Molecular Immunology of Porto University (IPATIMUP), Porto, Portugal exposed cells growing in laboratory to extracts of S. haematobium looking for changes, particularly in those traits associated with cancerous processes. In fact, cancer cells can be defined by rapid uncontrolled division, high resistance to death and - in the late stages of the disease - an abnormal capability to migrate through tissues (normal cells, except for a few exceptions, are not capable of move out of their “home” tissue/organ).

Botelho and colleagues found that, in fact, cells exposed to S. haematobium cells divided faster and more than those not exposed to the parasite, and also died much less. When searching for molecular clues to explain such alterations, it was found that the altered cells presented increased levels of bcl2 - a protein involved in cellular death and inked to cancer - while a tumour suppressor protein called p27 was reduced. These cells were also more mobile than controls, a crucial characteristic for metastasis formation. These results revealed S. haematobium as capable to induce the formation of cancer-like cells.

Next, in a second study[2], Botelho and colleagues injected S. haematobium - exposed cells into mice with no immune system - so to better observe the effect of the introduced cells - and, remarkably, this led to tumours extremely similar to those found in bladder cancer.

Crucially, animals injected with non-exposed cells showed no growths.

The connection between chronic infection by parasites and cancer is not unique to S. haematobium with the best know examples including Helicobacter pylori chronic gastric infection and stomach cancer or human papill oma viruses and hepatitis-C virus, which are associated respectively to cervix and liver cancer. Still, the knowledge of the mechanisms by which parasites lead to the malignant transformation of the host cells remains unclear. One of the main hypothesis suggests that the inflammatory process associated with chronic infections leads to the release of toxic molecules that affect the genetic stability of the surrounding cells, and eventual leads to the malignant transformations.

What Botelho's work reveals is a simple protocol to approach this question, which can be adapted to other parasitic infection and their associated cancers. Crucially their work manages to identify some of the molecules and pathways involved in the cancerous changes, suggesting that these could be target in therapies to prevent the development of a variety of cancer in chronically infected patients.

More information:

1. International Journal for Parasitology Volume 39, Issue 10, August 2009, Pages 1083-1091 Schistosoma haematobium total antigen induces increased proliferation, migration and invasion, and decreases apoptosis of normal epithelial cells

2. International Journal of Experimental Pathology Volume 90 Issue 4, Pages 448 - 453 Published Online: 20 Jul 2009 Tumourigenic effect of Schistosoma haematobium total antigen in mammalian cells

Source: Porto University