Gene's novel role may provide key to treating liver and neurodegenerative diseases

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Scientists at Singapore's Bioprocessing Technology Institute (BTI) have made a novel discovery about how the gene, "Fas-apoptosis inhibitory molecule" (FAIM), protects both immune and liver cells from apoptosis, or programmed cell death.

Their research is published in the current journal *Cell Death and Differentiation*.

The scientists, Jianxin Huo, Ph.D., and Shengli Xu, Ph.D., also discovered that this process may possibly be manipulated for clinical application and proposed the first-to-be-published in-animal model to study the role of FAIM in detail.

FAIM triggers a mechanism that ultimately impedes an important pathway to apoptosis, which is mediated by a key protein called Fas. Using their mouse model, the scientists elucidated part of the sequence of molecular events that regulates Fas-mediated apoptosis.

They found that FAIM functioned as a key switch in the Fas cell death circuit, which could be turned up or down to prolong or decrease cell survival.

Therefore, in principle, this gene could make a good target for drug intervention in either liver cirrhosis in which the target is to prolong cell survival, or in cancer in which the goal is to induce tumour cell death.

BTI Scientific Director Lam Kong Peng, Ph.D., who heads the immunology group that conducted the research, said, "We had earlier identified FAIM to be valuable in increasing the yield of biologics, and that had been one of the main focuses of BTI's research until now. We were extremely pleased to be able to establish that FAIM's function is preserved across both liver and immune cells, as this underscores its critical role in regulating cell death in disease."

The immunology team at BTI, one of the research institutes sponsored by Singapore's A*STAR (Agency for Science, Technology and Research), aims to further characterize the role of FAIM in liver cancer and other debilitating diseases.

According to Drs. Huo and Xu, there is also significant existing evidence that FAIM prevents neuron death and promotes neural outgrowth.

They hypothesize that FAIM might play a role in neuron protection, making it a potential therapeutic target for neurodegenerative diseases such as Alzheimer's and Parkinson's. Eventually, the Singapore scientists hope to conduct drug screens on FAIM to determine how it can be used to prolong or delay cell survival, and provide solutions to a wide variety of human diseases.

Drs. Huo and Xu's interest in FAIM was sparked by the work of their colleagues in BTI's animal cell technology group, which since 2007 has been using FAIM to enhance the longevity of biologics-producing cells to increase their yield in bioreactors, which are vessels in which organisms are cultured, and biochemically active substances derived from them.

Biologics are medicinal products such as vaccines, allergenics, tissues and recombinant proteins that can be extracted from natural sources (human, animal, or microorganism) and produced by biotechnology

methods.

Curious about FAIM's role in immune cells, particularly its increased expression in activated B cells, key effectors of the human immune system responsible for fighting viruses and other pathogens that invade the body, the two scientists began developing the first in vivo knockout mouse model to closely examine FAIM's role in preventing programmed cell death.

BTI Executive Director Miranda Yap, Ph.D., said, "The Immunology Group's venturing beyond the traditional boundaries of applied science has paid off with their discovery of a second role for FAIM in the seemingly unrelated field of immunology. Their work is indeed a fine example of how our scientists are constantly pushing the envelope to keep at the forefront of biomedical research."

More information: The *Cell Death and Differentiation* paper, "Genetic deletion of faim reveals its role in modulating c-FLIP expression during CD95-mediated apoptosis of lymphocytes and hepatocytes," is authored by: J. Huo, S. Xu, K. Guo, Q. Zeng and K-P Lam.

Source: Agency for Science, Technology and Research (A*STAR)