COMPLETION REPORT

Adaption of the Strategy Used to Prevent Schistosoma Japanicum Infection in Japanese Patients to our Current Study Involving Schistosoma Mansoni That Can Lead to Colorectal Cancer

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Schistosomiasis is a neglected disease caused by parasite infection that is endemic in many tropical and sub-tropical countries. People who are exposed to a source of water contaminated with faeces and parasite eggs that hatch in water will be infected with the disease. China and Japan had endemic Schistosomiasis at one time. Today, China, particularly in the coastal plain of the country still suffers from the infection, while Japan does not. A strategy to control and eradicate Schistosoma infection in Japan was *via* the used of Praziquantel. However, Praziquantel is the formulation for adults. Proper treatment of preschool-aged children infected with this disease is hampered due to the lack of a suitable paediatric dosage form to children. Indeed, the use of this drug may not be affordable to the poor. As the disease mainly occurs in the people and children living in the areas of poor drainage, it apparently gets little attention and support worldwide due to some political and geographical issues. This phenomenon motivates us to investigate the suitability of the drug to treat and control Schistosoma because the infection may contribute to an increased risk of colorectal cancer. Our present project proposes to adapt the prevention strategy on *Schistosomal japonicum* that had been used in Japan for our study involving *Schistosomal mansoni*. Clusterin was detected that overexpressed in the serum of colorectal cancer patients infected with *S. mansoni* from the endemic region in our previous study. Thus, Clusterin maybe the target for our low dosage form or drug-free strategy discovery for the treatment of Schistosoma infection.

Transfecting Clusterin into the low expressing colorectal cancer cells (HT29 and HCT116) was found less effective in this study. To reduce the research cost, the Clusterin-overexpressing colorectal cancer cells (SW480, SW620 and Caco2) were used, instead. Our study demonstrated that treatment of SW480, SW620 and Caco2 with Praziquantel induced cytotoxicity of the cancer cells by LDH cytotoxicity assay. This event was similar to the reduction in the growth of SW480, SW620 and Caco2 induced by silencing Clusterin in the cancer cells. Consistently, both events (Praziquantel treatment and Clusterin silencing) did not induce apoptosis, and only little cell cycle arrest was affected by Flow cytometry analyses. However, both events reduced the migratory activity of the Clusterin-silenced cancer cells as assessed by Wound healing assay. The detection of proliferation-associated protein in Praziquantel-treated cancer cells by Western blotting was not successful, but both events were found to decrease the mRNA expressions of FGF4 and BNIP3 in the cancer cells by Real-time PCR.

As both events produce similar mechanisms, the concentration of Praziquantel used for the disease treatment is expected can be reduced by combining Clusterin silencing along with the lower concentration use of Praziquantel. The study facilitates new estimation of Praziquantel concentration to reduce colorectal cancer and formulate suitable paediatric dosage form for children infected with this disease. Perhaps, a drug-free strategy for the treatment of the disease will be found one day. This project tailor the new drug prescription or strategy of the use of Praziquantel by combining the drug with specific gene silencing, which is suitable for children and affordable by the bottom billion in the developing countries.

Publication of the Results of Research Project:

Verbal Presentation (Date, Venue, Name of Conference, Title of Presentation, Presenter, etc.)

A verbal presentation will be made by the award recipient (Dr. Khoo Boon Yin) in the 3rd Advanced Medical and Dental Institute (AMDI) International Biohealth Science Conference (IBSC) on "Emerging Infectious Diseases" early next year at Hotel Riverside Majestic Kuching, Sarawak. The title of the presentation will be determined later. Tentative date of the conference will be on 18-20 January 2018.

Thesis (name of journal and its date, title and author of thesis, etc.)

Thesis

Eshtiyag Abdalla Abdalkareem. Identification of specific proteins from the serum samples of *Schistosoma mansoni* colorectal cancer patients, and the effects of IL-21 and Clusterin on human colorectal cancer cells. Viva-voce on 10 August 2016, Universiti Sains Malaysia.

Journal

Eshtiyag Abdalla Abdalkareem, Lim Boon Huat, Khoo Boon Yin (2017) Neutralising FGF4 protein in conditioned medium of IL21-silenced HCT116 cells restores the invasiveness of the colorectal cancer cells. Cytotechnology, CYTO-D-17-00069R1 under revisions.

Book (Publisher and Date of the Book, Title and Author of the Book, etc.)

None