

Two proteins involved in schistosome epigenetics play key roles in parasite's biology

June 28 2018



Methyl-CpG binding (SmMBD2/3) and chromobox (SmCBX) proteins are required for neoblast proliferation in the pathogenic blood fluke *Schistosoma mansoni*. Credit: Hoffmann et al. (2018)

Two proteins that recognize and translate DNA methylation marks in *Schistosoma mansoni* are required for growth of adult stem cells in the parasitic flatworm, as well as production of eggs, according to new research presented in *PLOS Pathogens* by Kathrin Geyer and colleagues at Aberystwyth University, U.K.

Schistosomiasis is a disease of varying severity caused by several species of parasitic flatworms known as schistosomes. More than 200 million people in developing countries are infected, with thousands dying every year. Existing drugs can treat schistosomiasis, but do not adequately



prevent reinfection or spread of the disease, so alternative strategies to target the parasites are needed.

In previous work, Geyer and colleagues demonstrated the importance of DNA methylation in <u>schistosome</u> biology, suggesting that this process could be important for development of new drugs. In DNA methylation, proteins add molecular components called <u>methyl</u> groups to DNA molecules, influencing genetic activity without affecting the underlying DNA sequence.

In the new study, the researchers conducted a series of experiments to further illuminate the activity of proteins involved in recognizing and translating these DNA methylation marks in the schistosome species *S. mansoni*. The experiments included use of a technique called RNA interference to reduce expression of genes coding for two proteins known to be involved in DNA methylation processes: methyl-CpG-binding (SmMBD2/3) and chromobox (SmCBX) proteins.

The experiments revealed details of SmMBD2/3 activity in schistosome cells and showed that it interacts with SmCBX. Disruption of SmMBD2/3 or SmCBX expression resulted in reduction of the number of proliferating <u>adult stem cells</u>, an important pool of cells in the parasites—and reduction in the number of eggs laid by the flatworms.

The lead author, Karl Hoffmann, states: "Our study provides further evidence for a functional DNA methylation system in schistosomes. While the full complement of participants have yet to be revealed, we have for the first time, within this group of animals, shown a clear link between DNA methylation and downstream processes."

These results suggest that SmMBD2/3 and SmCBX play essential roles in the biology of *S. mansoni*, especially considering that egg production is a key step in human pathology and disease transmission. Therefore,



drug development efforts could focus on disrupting the activity of these two proteins or their interaction with each other.

More information: Geyer KK, Munshi SE, Whiteland HL, Fernandez-Fuentes N, Phillips DW, Hoffmann KF (2018) Methyl-CpG-binding (SmMBD2/3) and chromobox (SmCBX) proteins are required for neoblast proliferation and oviposition in the parasitic blood fluke Schistosoma mansoni. *PLoS Pathog* 14(6): e1007107. <u>doi.org/10.1371/journal.ppat.1007107</u>

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Citation: Two proteins involved in schistosome epigenetics play key roles in parasite's biology (2018, June 28) retrieved 13 May 2024 from <u>https://medicalxpress.com/news/2018-06-proteins-involved-schistosome-epigenetics-key.html</u>

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