Both Aflatoxin B1 (AFB1) and the Liver fluke, *Opisthorchis Viverrini*, are known to cause liver cancer. Exposure to both of them simultaneously increases the risk of cancer strongly and synergistically. The mechanism for the synergistic effect is not clear.

To exert its carcinogenic effects, AFB1 needs to be metabolically activated to a genotoxic, DNA binding epoxide. We have demonstrated that the metabolic activation is catalysed by xenobiotic metabolising Cytochrome P450 2A (CYP2A) enzymes (CYP2A5 in mouse and CYP2A6 in humans). In cells where the CYP2A expression is high, a massive DNA binding of AFB1 takes place when exposed to the carcinogen.

We have also shown that, microbial infestation (viral, bacterial or parasitic) induces the CYP2A enzymes both in experimental animals and in humans. In our recent studies we have shown that the induction of the CYP2A genes is regulated by oxidative stress activated transcription factor NRF2. Hence, it is likely that the microbial infestation is not the cause of CYP2A induction *per se*, but rather the inflammation and associated oxidative stress conditions, which are the consequence of infestation. A particularly strong induction of the human CYP2A6 enzyme has been shown in infected individuals with a reduced endogenous antioxidant capacity due to a defective Glutathione-S-transferase T1 or M1 gene (GSTT1, GSTM1).

Based on these results we propose a mechanism for the synergistic effect of AFB1 and the *Opisthorchis Viverrini* in hepatocellular carcinoma where the Liver fluke infestation leads to inflammation and increased reactive oxygen species production. This will lead to NRF2 driven induction of the CYP2A6 and increased metabolic activation of AFB1 in exposed individuals. In people with a defective GST gene (about 15-40% of the population), the induction of the CYP2A6 and the metabolic activation of AFB1 will be particularly strong upon liver fluke infestation, and the risk for encountering liver cancer, particularly high.