

## **Development of Genetic Markers for Early Detection and Monitoring of Ivermectin Resistance in *Onchocerca volvulus* and Standardization of Molecular Assay for Identification of *Onchocerca* spp. (Osei-Atweneboana: Extension)**

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The continued success of onchocerciasis control and elimination programmes worldwide is largely dependent on sustained efficacy of ivermectin (IVM), which remains the only drug available for the control of the disease. However, recent reports show sub-optimal responses to IVM treatment and evidence of genetic selection in *Onchocerca volvulus*, raising concerns about the possible emergence of IVM resistance. We have carried out a fifteen month epidemiological study, involving skin microfilariae assessment and nodulectomies at day 90 after treatment and a parallel vector sampling across 30 onchocerciasis endemic communities in Ghana. Genetic analysis have been carried out on *O. volvulus* samples obtained from the epidemiological study, single nucleotide polymorphisms (SNPs) were identified in  $\beta$ -tubulin that are associated with poor IVM response phenotypes. A specific genotype configuration occurring at four SNP sites was found to be strongly associated with poor IVM response phenotype worms. Also we found three other SNPs occurring at three consecutive nucleotides positions. However, IVM resistance is suggested to be polygenic. Therefore in addition to the  $\beta$ -tubulin gene, genetic analysis will be carried out on GABA receptor HG1, involved in the mechanism of IVM resistance in veterinary parasitic nematodes. The genomic DNA sequences of HG1 gene will be analyzed and a number of loci under selection and SNPs that are found to be linked to poor IVM response phenotype worms will be selected as potential markers for evaluation and validation. The markers showing the highest consistent pattern of SNP-selection associated with poor IVM response phenotype worms will be used to develop a small panel of markers as a diagnostic tool for early detection and monitoring of IVM resistance. Available molecular assays will be standardized for identification of *Onchocerca* species present in vectors populations to provide a reliable interpretation of infection rates in man-biting blackflies.

### **Projektbeteiligte**

**Prof. Dr. Bernhard Fleischer**

Bernhard-Nocht-Institut  
für Tropenmedizin (BNITM)  
Hamburg

**Dr. Mike Yaw Osei-Atweneboana**

Council for Scientific and  
Industrial Research (CSIR)  
Department of Environmental Biology and Health  
Water Research Institute  
Achimota, Accra  
Ghana