A microarray-based system for the simultaneous analysis of single nucleotide polymorphisms in human genes involved in the metabolism of anti-malarial drugs

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Author(s) Hodel, Eva Maria; Ley, Serej D; Qi, Weihong; Ariey, Frédéric; Genton, Blaise; Beck, Hans-Peter
Author(s) at UniBasel Beck, Hans-Peter ; Hodel, Eva Maria ; Genton, Blaise ;
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BACKGROUND: In order to provide a cost-effective tool to analyse pharmacogenetic markers in malaria treatment, DNA microarray technology was compared with sequencing of polymerase chain reaction (PCR) fragments to detect single nucleotide polymorphisms (SNPs) in a larger number of samples. METHODS: The microarray was developed to affordably generate SNP data of genes encoding the human cytochrome P450 enzyme family (CYP) and N-acetyltransferase-2 (NAT2) involved in anti-malarial drug metabolisms and with known polymorphisms, i.e. CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, and NAT2. RESULTS: For some SNPs, i.e. CYP2A6*2, CYP2B6*5, CYP2C8*3, CYP2C9*3/*5, CYP2C19*3, CYP2D6*4 and NAT2*6/*7/*14, agreement between both techniques ranged from substantial to almost perfect (kappa index between 0.61 and 1.00), whilst for other SNPs a large variability from slight to substantial agreement (kappa index between 0.39 and 1.00) was found, e.g. CYP2D6*17 (2850C>T), CYP3A4*1B and CYP3A5*3. CONCLUSION: The major limit of the microarray technology for this purpose was lack of robustness and with a large number of missing data or with incorrect specificity

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