



## Stable Ischemic Heart Disease

### MRP4 EXPRESSION IN PLATELET OF PATIENTS UNDER CHRONIC ASPIRIN TREATMENT IS INFLUENCED BY MICRORNA MODULATION: A NEW MECHANISM FOR ASPIRIN RESISTANCE?

Poster Contributions  
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**Background:** Multidrug resistance protein-4 is an ATP Binding Cassette membrane transporter, actively involved in the efflux of important pharmacological and physiological compounds. It is found on platelet membrane and its over-expression has been show to induce aspirin (ASA) resistance in patients after by-pass surgery. MicroRNA (mir)-124a and mir-506 are able to down-regulate MRP4 in HEK 293 cell line. MicroRNA are small molecule of non-coding RNA involved in the regulation of many physiological and pathophysiological pathway. Platelet microRNA are involved in the regulation of several platelet activity and genes. Moreover these molecules are modulated by different drugs included aspirin. As Connections between MRP4, ASA and microRNA have not been elucidated in vitro or in vivo, thus the aim of the study was to investigate the role of microRNA on MRP4 modulation in patients under aspirin treatment.

**Methods and Results:** MRP4 mRNA expression was analyzed by RealTime PCR in a platelet samples of 25 healthy controls without ASA treatment, 25 CV patients in ASA treatment (100mg/die) for 1-month and 25 after 3-month ASA treatment. The 3-month ASA group showed a significant higher expression of MRP4 mRNA compared to the control group ( $p < 0.005$ ). The ASA 1-month cohort had mRNAs level comparable to the control group. A panel of 174 microRNA were run on the pool of each cohort. Between the modulated microRNA 26b-5p, which target MRP4, was found significantly down-regulated in the two cohort under aspirin treatment,

**Conclusion:** This is the first evidence that MRP4 mRNA is induced in humans under aspirin treatment. Moreover, we found in our study that all the microRNA targeting platelet aggregation genes are down-regulated. These evidences suggest that microRNAs are involved in MRP4 modulation in patients under ASA treatment and therefore may also be involved in mechanism associated with ASA resistance.