In-vivo and _in-vitro_ investigation of Asprin using pan genomic differential gene expression analysis.

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Aspirin is a non-steroid anti-inflammatory drug known to inhibit NF-kappaB activation and the expression of associated gene expression of e.g. cyclooxygenase-2 (COX-2), iNOS, VCAM-1 and ICAM-1 (Jung et al., 2006) in aged rats. Aspirin is known to display a wide range of side-effects which can be partly explain by its action on many different key signaling components such as MCP-1, ROS and AP-1 (Dragomir et al., 2006); scavenger receptor class B type I as well as promoting cholesterol efflux (Tancevski et al., 2006); metalloprotease 2 (Nicolae et al., 2005), and apoptosis via BCL2 down-regulation (Kim et al., 2005).

In this study, we set up to investigate the effect of aspirin on gene expression *in-vivo*. Widely utilized acetyl salicylic acid has been used as a prominent sample to illustrate microarray- based characterization of gene activity changes and changes in signalling induced by drugs.
Experiments were performed using human monocytes, *in-vitro* stimulated with 200 µM Aspirin. Expression changes were also examined after intravenous (1g) administration to healthy human volunteers.
After RNA extraction, samples were analyzed with an Illumina station employing Human-6 v2 Expression BeadChips containing 6 arrays with 48 000 probes each.

In the cell experiment, 442 probes indicated expression changes higher than factor 3, 45 were identified which showed more than 20-fold changes. Altered gene activities comprise e.g. PI3 a gene encoding an elastase-specific inhibitor or MMP7, a gene encoding Proteins of the matrix metalloproteinase (MMP) family involved in the breakdown of extracellular matrix.

Four h after i.v. administration, 168 probes indicated more than 3-fold, 17 more than 10-fold changes including e.g. CXCR4, a gene encoding a CXC chemokine receptor specific for stromal cell-derived factor-1.
The Ingenuity software was used to display networks of potential interactions and to analyze links to the agent's pharmacological activity profile.
These data indicate that pan genomic microarray analysis, beyond being useful for molecular characterization of drug activities, gives clues to mechanisms of action.