INTRODUCTION
Breast cancer is a major cause of cancer death in women worldwide. Experimental and epidemiological studies indicate that natural chemopreventive agents like resveratrol may act as chemopreventive agents and inhibit mammary carcinogenesis. The antiproliferative property of RES has been demonstrated in vitro against breast cancer cells due to the induction of apoptosis via down-regulation of NF-kappa B, anti-apoptotic genes and inhibition of survival oncogenes. The antiproliferative potential of resveratrol and its analogs has been shown to be dose-dependent and similar in both cell lines. The results obtained for MCF-7 cells were chosen to demonstrate the metabolic effects of resveratrol on mammary carcinoma cells.

RESULTS & DISCUSSION
Resveratrol induced degradation or release of amino acids (Fig. 3). Enzymatic conversion of tryptophan to bioactive metabolites serotonin was stimulated, whereas methionine undergoes increased non-enzymatical oxidation to methionine-sulfoxide. Taurine, on the other hand, was substantially released from the cells, which is often linked with cell swelling and the occurrence of reactive oxygen species (Lambert, 2007).

Polyamines: Up toresveratrol treatment with a profound modulation of polyamines biosynthesis, could be seen in mammary cancer cells (Fig. 4). While the synthesis of polyamines from ornithine by ornithine decarboxylase, seemed to be inhibited, an up to 8-fold increased synthesis of spermidine from putrescine was observed indicating inhibition of spermine synthase. Interestingly, synthesis of spermine from spermidine was not stimulated, but rather inhibited. Putrescine and spermidine are essential for a variety of cellular processes related to signal transduction, growth and differentiation.

Therefore, resveratrol-induced changes in polyamine metabolism could be directly linked to cell fate decisions (Takagi et al, 2006). Conversion of putrescine to metabolically active spermidine and spermine occurs via two pathways, one of the two rate-limiting enzymes of polyamines metabolism, spermidine synthase (SDC) and S-adenosylmethionine decarboxylase (SADMC). While SDC is involved in the proliferation of cells (Movic et al, 2000) Resveratrol and the analog (-)-3,5,4′-trimethoxystilbene have been shown to reduce SDC and SADMC activities by depletion of the polyamines putrescine and spermidine, hence exerting the cytotoxic effects by depletion the intracellular pool of polyamines (Wolter et al, 2003; Schneider et al, 2003).

Arachidonic acid: A profound increase in eicosanoids from arachidonic acid (AA) and its metabolite 12(S)-HETE could be observed with high doses of resveratrol (Fig. 5). AA is released from cell membranes from arachidonic acid via activation of phospholipase A2, and subsequently converted to 12(S)-HETE by the action of 12-lipoxygenase. Increased levels of 12(S)-HETE may therefore indicate oxidative stress in tumor cells under resveratrol treatment (Nazarewicz et al, 2007). Furthermore, resveratrol also reduced prostaglandin E2 (PGE2) levels from 4 to 0 pg/ml cells, thus confirming that this polyphenol is an inhibitor of cyclooxygenase 2 (Murias et al, 2000).

CONCLUSION
The metabolic effects of resveratrol on breast cancer cell lines could be revealed using targeted metabolomics. Bioactive amines and polyamines, namely serotonin, putrescine, spermidine, and methionine-sulf oxide, as well as arachidonic acid and its metabolite 12(S)-HETE were identified as potential markers for the pharmacological response of resveratrol, which must be considered in humans following oral uptake of dietary resveratrol or of other substances intended to be chemopreventive agents.

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