

## **Abstract Dissertation Beatrix Amann**

(„Untersuchung schädigender Einflüsse unterschiedlicher Bismut-Spezies auf die physiologische Darmmicrobiota unter besonderer Berücksichtigung von methylierten Derivaten“)

*Investigation of inhibiting influences of various bismuth species to the physiological intestinal microbiota under a special regard of methylated derivatives*

Various bismuth species inhibit the growth of *B. thetaiotaomicron*, a dominant member of the intestinal microbiota, but with different power: Growth inhibition of colloidal bismuth subcitrate (CBS) is induced at  $\mu\text{M}$ -concentration, whereas growth inhibition takes place by exposure of the methylated bismuth species like mono- (MMBI), dimethyl- (DMBI), and trimethylbismuth (TMBi) already at nM-concentration (TMBi:  $\text{MIC}_{50} = 30 \text{ nM}$ ).

The toxicity increases with increasing number of methyl groups in the order  $\text{MMBI} < \text{DMBI} < \text{TMBi}$ . The exposure of TMBi or CBS leads to an irreversible growth inhibition, whereas the partially methylated bismuth derivatives causes reversible growth inhibition, probably due to their lesser stability.

For studying the molecular background of this growth inhibition, we compared several biochemical constituents in the absence and presence of TMBi such as the lipid composition of the cell membranes, as well the composition of the proteins and transcripts. It has been shown that the influence of TMBi to *B. thetaiotaomicron* may cause a multifactorial disorder, which induces the changed growth behavior. Thus, the transcription of lipid biosynthesis, polysaccharide biosynthesis and cell wall biogenesis is in the presence of TMBi strikingly reduced. On the contrary, genes which are obviously involved in processes, which catalyze recombination of DNA are preferentially expressed and therefore indicate that damaged DNA could occur upon the addition of TMBi, which must be subsequently exchanged.

Finally, the apparently TMBi-modified putative chaperone Skp, which has an important influence on the composition of the outer membrane and therefore disturbs its function, could be the main cause for the reduced growth of *B. thetaiotaomicron* upon addition of TMBi.