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Mycolic acid biosynthesis in *Rhodococcus erythropolis*

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Oil contamination is one of the most hazardous environmental pollutions. There were numerous oil spills in the last three decades. Oil tanker accidents and oil-rig catastrophes are still reported. Oil spills had great impact on the wildlife as well as on the economy by cutting down the agriculture, food industry and tourism.

Surfactants are useful weapons in the war against oil pollution. They are suitable to solubilize hydrophobic materials, consequently to clean oil tanks and pipes. In addition they can be used for emulsification of animal fats in food industrial and housekeeping wastewaters. Many bacteria can produce substantial amount of biosurfactants which can promote the solubilization of hydrophobic hydrocarbons, thus these bacteria themselves or the native microflora can utilize the unctuous pollutants. An additional advantage of the biosurfactants over the synthetic surface active molecules is that these compounds are easily biodegradable, they don't persist in the environment.

A special biosurfactant group is composed of mycolic acids which are basically α-alkyl, β-hydroxy fatty acids. Mycolic acids are the most characteristic components of the cell wall of the so called mycolata bacterial group. This group belongs to the Actinomycetales and contains the genera *Mycobacterium*, *Corynebacterium*, *Nocardia*, *Rhodococcus* and others.

A Gram+ bacterium, Rhodococcus erythropolis MK1 strain has been isolated from polluted soil in our lab. The cells grown in the precence of hydrocarbons produced cell-wall-bound surfactants in order to make oils accessible. Based on the literature and preliminary gas chromatographic analysis, this surface active compound seemed to be trehalomycolate. Although, the mycolic acid biosynthesis was already characterized in the pathogenic Mycobacteria, the biosynthetic routes of trehalomycolate in Rhodococcales are less known. Therefore, we aimed to map the mycolic acid biosynthesis pathway in Rhodococcus erythropolis strains. First, we sequenced the genome of our strain by SOLID™ next generation DNA sequencer. The reads were mapped on the R. erythropolis PR4 genome in the NCBI database. We searched for rhodococcal homologs of the known mycobacterial and corynebacterial genes involved in mycolic acid biosynthesis. We found conserved regions in the genome which are likely responsible for the biosynthesis of mycolic acids. Nevertheless, differences in the biosynthetic pathways can also be recognized. The ongoing comparative whole genome transcript analysis discloses the genes really necessary for the anabolism of trehalomycolates. This knowledge will be used for constructing strains for biotechnological applications.

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Chronic hypertriglyceridemia induces early tau hyperphosphorylation and impaired long term potentiation in apoB-100 transgenic mice

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Alzheimer's disease (AD) is the commonest form of dementia and affects more than 32 million people worldwide. Epidemiological studies confirmed the importance of vascular dementia as the second most common cause of dementia in the elderly, representing 15–20% of all cases of dementia. These figures threaten to rise as the population ages unless efficient preventative measures are introduced.

The role of hyperlipidemia in the development of vascular dementia and cognitive decline is still controversial. Recent studies indicate that ApoB-100-induced hyperlipidemia and atherosclerosis are not only implicated in the pathogenesis of cardiovascular diseases but may also affect the cerebrovascular system thus contribute to the development of neurodegenerative disorders. Other studies have shown that AD is accompanied by an elevation in apolipoprotein B concentration in the serum. It was also demonstrated, that progressive cognitive impairment in AD is accompanied by neurovascular dysfunction.

To further clarify the possible role of hyperlipidemia in the development of neurodegeneration and dementia we have generated transgenic mice overexpressing the human ApoB-100 protein. Transgenic mice fed a regular chow diet show elevated serum triglyceride levels, fed a cholesterol rich diet show hypercholesterolemia leading to coronary and systemic atherosclerosis by the age of 6 months. Previously, we have shown that microcapillary density significantly decreases in the cortex of hyperlipidemic (hypertriglyceridemic and hypercholesterolemic) transgenic mice.

Here we show, that adult transgenic mice (6 months old) present significantly elevated cerebral level of triglycerides and ApoB-100 indicating the dysfunction of blood-brain barrier. Moreover, in aging transgenic mice (10 months old) triglyceride-rich lipid-droplets in the cortex can be detected. The level of ApoE, the major lipid transporter molecule in the brain was also significantly increased in adult transgenic brains. Under pathological conditions (e.g. AD) the Tau protein becomes hyperphosphorylated, which leads to dynamic instability and disintegration of microtubular network and eventually to the formation of neurofibrillary tangles (NFT). Tau phosphorylation patterns in the brain of 3 and 6 month old transgenic animals were investigated using several phosphosite-specific antibodies (Ser^{199}, $Ser199/^{202}$, Ser^{262},