# ABSTRACT

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Title of diploma thesis: **Study of microstructure of skin barrier model using deuterated ceramides**

Ceramides (Cer) are sphingolipids, which participate in eucaryotic cells in various biological processes (cell signalling, proliferation, differentiation and cell apoptosis). In mammalian skin, Cer are localized in the uppermost layer of epidermis, *stratum corneum* (SC). In this layer, Cer along with cholesterol (Chol) and free fatty acids form multilayer lamellae of intercellular lipid matrix.

The skin lipid arrangement in SC is still unclear. To evaluate the skin lipid arrangement, skin membrane models with labelled (deuterated) lipids have been used. Therefore, the aim of this work was to synthesize sphingosine with deuterated chain and Cer based on deuterated sphingosine, *i.e., N*-lignoceroyl sphingosine-$d_{28}$ (with lignoceric acid acyl (C24); *d*-CerNS) and *N*-lignoceroyl-$d_{47}$ sphingosine-$d_{28}$ (*dd*-CerNS) and to study their phase behaviour and arrangement in model membranes by using biophysical studies.

Synthesis of deuterated Cer started from elimination of 1-pentadecanol-$d_{31}$ to obtain a deuterated terminal alkene. Next, a vinylation of (*S*)-Garner´s aldehyde led to obtain an intermediate, which was treated in Grubbs´ metathesis with terminal alkene. The product of Grubbs metathesis (a protected deuterated sphingosine) was then deprotected under acid conditions; free sphingoid base was acylated by protonated or deuterated lignoceric acid using water soluble carbodiimide. Synthesized *d*-CerNS and *dd*-CerNS were incorporated into SC membrane models. Model mixtures contained *d*-CerNS or *dd*-CerNS, (deuterated) lignoceric acid and Chol in 1:1:1 molar ratio with an addition of cholesteryl sulfate (5 wt%). Overall, four types of model membranes with different representation of deuterated methylene ($CD_2$) chains, were studied by temperature depended infrared spectroscopy at temperature from 28°C to 100°C. A phase behaviour (conformation, lateral arrangement, and miscibility) of

model lipid membranes was investigated. The results of this study could be helpful in explaining the (patho)physiological arrangement of SC lipids.