Doctoral thesis to be defended today: Title ‘’Tumor response mechanisms and treatment effects of alpha1-oleate’’

Hamlet BioPharma, the pharmaceutical company, specializing in the development of drugs for cancer and infections, announces the PhD thesis defense by Samudra Sabari, M. Sc. The defense will take place at 1 pm, Belfragesalen, BMC D15, Lund. The Faculty opponent will be Professor Boris Zhivotovsky, Karolinska Institutet.

The thesis is based on four papers, three of which are published in peer reviewed international journals and one manuscript**.**

The first paper describes a new concept for cell death, where Alpha1H targets a major membrane system (ER) in tumor cells that stretches from the cell border all the way to the nuclei. Organized like a "fishing net" this membrane defines many aspects of cellular life, including cell death. The paper proposes that the ER allows dying tissues to capture cellular contents, to avoid leakage of toxic components to the surrounding tissue during the cell death process. This mechanism could be an essential explanation for the low toxicity of the alpha1H complex, which has been seen in cells, animal models and patients. http://www.life-science-alliance.org/content/8/6/e202403114

The second paper describes the clinical study of Alpha1H in patients with bladder cancer, specifically the effects of increasing doses on the tumor response. Over the course of the treatment, the tumor number and size were significantly reduced. Outcome- Strong, dose-dependent anti-tumor effects were detected in Alpha1H-treated patients, for a combination of clinical and molecular endpoints. Treatment resulted in a complete or partial response in 82% of the tumors treated with the higher dose and in 45% treated with the lower dose of Alpha1H.

http://onlinelibrary.wiley.com/doi/10.1002/cam4.70149

The third paper investigates the mechanism behind the rapid shedding of tumor cells, that occurs in patients treated with Alpha1H**.** The treatment triggers rapid shedding of tumor cells and tumor fragments into the urine, suggesting that the cell adhesion machinery of the tumor is targeted by the treatment. The study shows that alpha1-oleate affects specific cell adhesion mechanisms, using cancer cell cultures and biopsies from alpha1-oleate treated patients. A rapid disruption of multiple cell adhesion complexes was detected in alpha1-oleate treated cells, including focal adhesions, adherens junctions, tight junctions but not gap junctions and

desmosomes. *In manuscript.*

The fourth paper concerns combination therapy of Alpha1H and chemotherapeutic agents Mitomycin and Epirubicin in a murine model of bladder cancer. The results show that alpha1-oleate effectively inhibits bladder tumor progression in a murine model, both as a single treatment and in combination with low-dose chemotherapy. Repeated alpha1-oleate treatment reduced tumor burden, suppressed proliferation and angiogenesis markers, enhanced chemotherapeutic drug uptake, and promoted apoptosis. In addition, gene expression profiling indicated a shift toward a non-malignant transcriptomic pattern in treated bladders. These findings support the further development of alpha1-oleate as a therapeutic and preventive strategy for bladder cancer.

http://onlinelibrary.wiley.com/doi/10.1002/ijc.34500

‘’ We are delighted to see the work summarized in the form of a PhD thesis and look forward to a stimulating academic discussion of these important findings’’ says Professor Gabriela Godaly, main supervisor of Samudra Sabari.

‘’ The state-of the art imaging platform that we have built is showcased in this work’’ says Arunima Chaudhuri, research scientist and co-supervisor of Samudra Sabari.

For further information, please contact:

Catharina Svanborg, Chairman and Founder of Hamlet BioPharma,
+46-709 42 65 49 catharina.svanborg@hamletpharma.com

www.hamletbiopharma.com