"Regulation and function of adapter proteins NTAL and LIME in *Helicobacter pylori*-infected epithelial cells"

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The human microbial pathogen *H. pylori* colonises the gastric mucosa and represents a risk factor for developing chronic gastritis, peptic ulcer diseases or even gastric adenocarcinoma. It is supposed that *H. pylori* abuses lipid raft domains on the host cell plasma membrane to infect the cell. Investigating lipid raft molecules by a screen with a number of different antibodies the adapter protein NTAL was identified in DRM-fractions of AGS cells. NTAL is one of four known lipid raft-associated transmembrane adapter proteins (TRAPs) that up to now were exclusively described to mediate signal propagation downstream of antigen receptors. These results posed the question, whether TRAPs adopt a role in *H. pylori*-infected epithelial cells, too. In summary the following results were obtained:

I. All lipid raft-associated TRAPs that are known so far (LAT, PAG, NTAL and LIME) are expressed in HCA-7 cells. However expression levels are quite low compared to peripheric blood mononuclear cells.

II. The studies revealed that *H. pylori* induces tyrosine phosphorylation of NTAL as well as LIME within 5-15 min of infection.

III. Further, it was observed that *H. pylori*-activated NTAL and LIME bind to the SH2-domain containing cytoplasmic adaptor proteins Grb2 and SHP2.

IV. In *H. pylori*-infected HCA-7 cells NTAL and LIME associate with the c-Met receptor. Moreover, NTAL and LIME inducibly interact with the EGFR.

V. NTAL has a contributory role in *H. pylori*-induced ERK-phosphorylation and influences ERK-dependent phosphorylation of $cPLA_2$.

These results indicate that in *H. pylori*-infected epithelial cells NTAL represents an important regulator of c-Met-mediated ERK-activation in lipid rafts. Metabolites of $cPLA_2$-generated arachidonic acid are pivotal mediators of the inflammatory response. Thus, the obtained results imply a functional role for NTAL in *H. pylori*-induced gastric inflammation.