4. Summary

4.1. CEACAM1 Isoforms

In rat PC12 cells, the CEACAM1-4L and CEACAM1-4S splice variants were detected. Additionally, two novel isoforms, CEACAM1-4C1 and CEACAM1-4C2 were identified. Both are secreted proteins. The C-terminus of CEACAM1-4C2 is identical to that of CEACAM1-4L, which allowed the specific detection of CEACAM1-4C2 on the protein level by an antiserum directed against the CEACAM1-4L cytoplasmic part. CEACAM1-4C2 was found both *in vitro* in conditioned cell culture medium from PC12 cells and *in vivo* in rat serum. In serum of animals with a growing Morris hepatoma, the CEACAM1-4C2 level was elevated.

4.2. CEACAM1-mediated Signal Transduction

CEACAM1 tyrosine phosphorylation was detectable after inhibition of cellular tyrosine phosphatases with the phosphatase inhibitor pervanadate.

The modulation of CEACAM1 macromolecular organisation by addition of antibodies was applied in order to induce a CEACAM1-specific stimulus. Treatment with the anti-CEACAM1 mAb Be 9.2 in combination with a secondary antibody caused the formation of large CEACAM1-clusters in the plasma membrane. Stimulation of CEACAM1 by clustering induced its fast and reversible tyrosine dephosphorylation.

The interaction of CEACAM1 with the tyrosine phosphatase SHP2 was directly influenced by this dephosphorylation: the interaction, which is dependent on CEACAM1 tyrosine phosphorylation, was reduced after stimulation.

The signal initiated at the membrane caused the reversible and specific activation of the MAP kinases ERK1 und ERK2. In contrast, the activity of the related kinases JNK and p38 remained unchanged.

Neuronal differentiation of PC12 cells with NGF reduced the constitutive level of CEACAM1 tyrosine phosphorylation and abolished further dephosphorylation upon stimulation of CEACAM1.

4.3. Interaction of CEACAM1 with the Actin Cytoskeleton

Stimulation by clustering caused CEACAM1 to bind to the actin cytoskeleton. An assay was established, in which the degree of insolubility of CEACAM1 after extraction of cells with the detergent Triton X-100 was calculated as a measure for its interaction with the actin cortex. The F-actin-destabilizing reagents cytochalasin D and latrunculin A significantly reduced the level of clustering-induced CEACAM1 detergent insolubility. The CEACAM1-actin-interaction was dependent on several aspects of the cellular state: both an increase in cell density as well as neuronal differentiation of PC12 cells induced a stronger interaction.

The level of CEACAM1 tyrosine phosphorylation had no influence on its interaction with actin. Contrary, an intact cytoskeleton was important for the regulation of CEACAM1 tyrosine phosphorylation.

The cytoplasmic part of CEACAM1 was dispensable for the clustering-induced binding to the actin cytoskeleton, demonstrated with a deletion mutant lacking the cytoplasmic tail.

Adversly, the colocalization of CEACAM1 and actin at cell contacts in Barbe endothelial cells was only detected for CEACAM1-4L.