Supplementary Figure Legends:

Supplementary Figure A. Involvement of presenilin 2 in N-cadherin processing.
Cell lysates from $PS1^{+/+}$, $PS1^{-/-}$ and $PS1/2^{-/-}$ MEFs were separated by ultracentrifugation in membrane (upper panel) and cytosolic proteins (lower panel). Fractions were subjected to Western blot analysis using C-terminal anti-N-cadherin antibodies. N-Cad/FL: full length N-cadherin; CTF: C-terminal fragment of N-cadherin.

Supplementary Figure B. Densitometric analysis of CTF production in different cell lines (Figure 1B, upper panel). CTF1 generation was calculated as percentage of total N-cadherin (full length N-cadherin plus CTF1).

Supplementary Figure C. Anti N-cadherin (C-terminal) immunoblot of proteins from three different $ADAM10^{-/-}$ and $ADAM10^{+/+}$ MEF cell lines. N-Cad/FL: full length N-cadherin; CTF: C-terminal fragment of N-cadherin.

Supplementary Figure D. Effect of metalloproteinase inhibitors on constitiutive N-cadherin cleavage. WT-MEFs were incubated with various concentrations of hydroxamate inhibitor GW280264X (ADAM10/TACE inhibitor), selective ADAM10 inhibitor GI254023X or vehicle control (dimethylsulfoxide, DMSO) for 4 hours in the presence of γ-secretase inhibitor (0,5μM) and analysed by Western blot. N-Cad/FL: full length N-cadherin; CTF: carboxyterminal fragment of N-cadherin.

Supplementary Figure E. Decrease of CTF1 is associated with decrease of CTF2. Wildtype fibroblasts were treated with ADAM10 inhibitor GI254023X (3 and 5 μM) or left untreated. After 16 h incubation, cell pellets were harvested and subjected to Western blot analysis with an anti C-terminal N-cadherin antibody. For densitometric analysis

CTF1 and CTF2 were quantificated and compared to the fragments of untreated cells (100 %). DMSO vehicle control looked similar than untreated cells (not shown).

Supplementary Figure F. N-cadherin co-precipitates with ADAM10.
Identical amounts of wildtype or ADAM10-deficient cell lysates were immunoprecipitated with anti-ADAM10 antibodies (IP:ADAM10) and loaded onto SDS-Page. The immunoblot was stained with anti-N-cadherin antibodies.

Supplementary Figure G. N-cadherin expression in ADAM10-deficient and wildtype embryos. A lateral and dorsal view of E9 embryos stained with an anti N-cadherin antibody (MNCD2). N-cadherin is predominantly expressed in the otic pit (Ot), in heart tube (Ht), in the somites (S) and in the neural tube (Nt). Bar: 500µm.

Supplementary Figure H. Efficiency of N-cadherin/b-catenin immunoprecipitation. Lysates of wildtype and ADAM10-deficient cells were subjected to immunoblotting before (lysate) and after immunoprecipitation (IP-lysate) and stained with the appropriate antibody.

Supplementary Figure I. Influence of β-catenin/TCF signalling on cyclin D1 expression and activity. Wildtype fibroblasts were transfected with empty vector pcDNA3 (-), β-catenin (+) or dominant negative (DN) TCF4 (+) each with a cyclin D1 reporter plasmid and the transfection control, renilla luciferase. After 48 h, the expression of cyclin D1 was assayed. Data are expressed as relative light units normalised to the co-transfected Renilla luciferase and show the relative luciferase activity as percentage of the control (empty vector). The same cell lysates were also analysed for cyclin D1 expression by immunoblot.

Supplementary Figure J. Influence of β-catenin overexpression on downstream genes. Wildtype and ADAM10-deficient cells were transfected with β-catenin. After 48 hours cells lysates were analysed for β-catenin expression by Western blotting. The immunoblot was reprobed with anti cyclin D1, c-myc, c-jun and tubulin (loading control) antibodies.

Supplementary Figure K. Ionomycin-increased cyclin D1 expression in wildtype cells is ADAM10 dependent. Wildtype and ADAM10-deficient cells were stimulated with 5μM ionomycin or vehicle control (DMSO) for different periods. Wildtype cells were additionally stimulated in the presence of ADAM10 inhibitor GI254023X (3μM). Cell pellets were harvested and analysed by Western blotting using anti-cyclin D1 antibodies. Since cyclin D1 expression in ADAM10-deficient MEFs was below the detection limit, a protein staining (ponceau S) is also shown.