

Curriculum Vitae

Prof. Dr. Dr. h.c. Christian Haass



BioMedical Center (BMC)

Ludwig-Maximilians-University München

&

German Center for Neurodegenerative Diseases (DZNE)

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Academic Education

1981-1985 studying Biology at the Ruprechts-Karls-University, Heidelberg.

Nov.1989 Ph.D. (*summa cum laude*)” cDNA cloning of proteasome subunits”.

Postdoctoral Training

1990-1992 Postdoctoral fellow in the laboratory of Prof. Dr. D. Selkoe at the Center for Neurologic Diseases /Harvard Medical School.

Advanced Professional Degrees

1993-1995 Assistant Professor of Neurology at the Harvard Medical School.

1995 Professor (C3) of Molecular Biology at the Central Institute of Mental Health, Mannheim (University of Heidelberg).

since 1999 Professor of Biochemistry (C4) and head of the Department of Metabolic Biochemistry at the Adolf-Butenandt Institute (Ludwig Maximilian University, Munich).

since 2009 Speaker of the German Center for Neurodegenerative Disorders (DZNE) in Munich.

Selected awards

1990 Award of the Heidelberg Society for Molecular Biology for the best Ph.D.

thesis

1996 Organon Research Award

1997 Award of the Heidelberg Academy of Sciences

2000 International Alois Alzheimer Award

2002 Family Hansen Award

Ernst Jung Award for Medicine

Gottfried Wilhelm Leibniz-Award of the Deutsche Forschungsgemeinschaft

Potamkin Award of the American Academy of Neurology

2006 MetLife Foundation Promising Award for Medical Research

Sheik Hamdan Award for Medical Sciences (in the category *Biology of Aging*)

Dittner Award for Alzheimer Research
2010 Honorary Degree of the University of Zurich
2012 ERC advanced grant
2014 Order of Merit on Ribbon from the Federal Republic of Germany
2015 MetLife Award for Medical Research
2016 Rolf Becker Award

Speaker of national and international Research Projects

- 1.) Speaker of the DFG-Forschungsschwerpunkt (National Priority Program)
“Cellular Mechanisms of Alzheimer's Disease”
- 2.) Speaker of the Sonderforschungsbereich 596 (Collaborative Research Center)
“Molecular Mechanisms of Neurodegeneration” since 2000.
- 3.) Work package leader of DIADEM (EU grant)
- 4.) Work package leader of APOPIS (EU grant)
- 5.) Member and sub-project speaker of the DFG Excellence Cluster "Center for Integrated Protein Science Munich" (CiPSM)
- 6.) Speaker of the DFG Excellence Cluster "Systems Neurology" (SyNergy)

Professional Memberships

Member of the Society for Neuroscience
Member of the Academia Europaea
Elected member of the European Molecular Biology Organization (EMBO)
2002 - 2008 Member of the Senate of the Deutsche Forschungsgemeinschaft (DFG)
Member of the board of the Alzheimer International Foundation
Member of the board of Hans und Ilse Breuer Foundation
Elected member of the Leopoldina
Elected member of the Bavarian Academy of Sciences and Humanities

Peer Reviewer

Nature, Nature Medicine, Nature Genetics, Nature Cell Biology, Nature Neuroscience, Nature Methods, Nature Review Journals, Science, Cell, Mol. Cell, Neuron, J. Biol. Chem., Biochemistry, J. Cell Biol., EMBO J., EMBO Molecular Medicine, EMBO Reports, Proc. Natl. Acad. Sci. USA, J. Neuroscience, Trends in Cell Biology, PLOS- Biology etc.

Memberships in Editorial Boards

- 2000-2005: Member of the Editorial Board of *J. Biol. Chem.*
- 2005-2010: Advisory Board Member of *EMBO Reports*
- since 2005: Advisory Board Member of the *EMBO J.*
- since 2005: Member of the Board of Reviewers of *Science*
- since 2008: Advisory Board Member of *EMBO Mol. Medicine*
- since 2012: Advisory Board Member of *J. Neuroscience*

Organization of International Conferences

Annual Eibsee Conference of the DFG Priority Program and the SFB 596 "Cellular Mechanisms of Alzheimer's Disease" (since 2000)

Titisee Conference of the Boehringer Ingelheim Foundation on "Alzheimer's and Parkinson's Disease: from basic science to therapeutic treatment"(19. - 23. 3. 2003)

SFB- Symposium on "Molecular Mechanisms of Neurodegeneration" (Wildbad Kreuth; 20. - 23. 7. 2003)

SFB- Symposium on "Regulated Intramembrane Proteolysis" (Schloss Ringberg; 27. - 30. 11. 2006)

SFB- Symposium on "Neurodegeneration in Zebrafish" (Schloss Ringberg 21. - 24. 2. 2010)

SFB- Symposium on "Mitochondria in Neurodegeneration" (Schloss Ringberg 6. - 9. 10. 2010)

EMBO Conference "Mechanisms of Neurodegeneration" (EMBL, Heidelberg, 2015)

EMBO Conference "Mechanisms of Neurodegeneration" (EMBL, Heidelberg, 2017)

Selected Publications (out of >300); H-Factor: 91

Suárez-Calvet M, Caballero MA, Kleinberger G, Bateman RJ, Fagan AM, Morris JC, Levin J, Danek A, Ewers M, Haass C for the Dominantly Inherited Alzheimer Network (2016) Early changes of CSF sTREM2 in Dominantly Inherited Alzheimer's Disease follow markers of Amyloid Deposition and Neuronal Injury. *Science Translational Medicine* in press.

Mori K, Nihei Y, Arzberger T, Zhou Q, Mackenzie IR, Hermann A, Hanisch F; German Consortium for Frontotemporal Lobar Degeneration; Bavarian Brain Banking Alliance, Kamp F, Nuscher B, Orozco D, Edbauer D, Haass C (2016) Reduced hnRNPA3 increases C9orf72 repeat RNA levels and dipeptide-repeat protein deposition *EMBO Rep.* 2016 Jul 26. pii: e201541724. [Epub ahead of print].

Xiang X, Werner G, Bohrmann B, Liesz A, Mazaheri F, Capell A, Feederle R, Knuesel I, Kleinberger G, Haass C (2016) TREM2 deficiency reduces the efficacy of immunotherapeutic amyloid clearance *EMBO Mol Med* 2016 Jul 8. pii: e201606370. doi: 10.15252/emmm.201606370. [Epub ahead of print].

Suárez-Calvet M, Kleinberger G, Caballero MA, Brendel M, Rominger A, Alcolea D, Fortea J, Lleó A, Blesa R, Gispert JD, Sánchez-Valle R, Antonell A, Rami L, Molinuevo JL, Brosseron F, Trschütz A, Heneka MT, Struyfs H, Engelborghs S, Sleegers K, Van Broeckhoven C, Zetterberg H, Nellgård B, Blennow K, Crispin A, Ewers M, Haass C (2016) CSF sTREM2 is increased in early symptomatic stages of Alzheimer's disease and associates with neuronal injury markers. *EMBO Mol Med* 8(5): 466-76.

Willem M, Tahirovic S, Busche MA, Ovsepian SV, Chafai M, Kootar S, Hornburg D, Evans LD, Moore S, Daria A, Hampel H, Muller V, Giudici C, Nuscher B, Wenninger-Weinzierl A, Kremmer E, Heneka MT, Thal DR, Giedraitis V, Lannfelt L, Muller U, Livesey FJ, Meissner F, Herms J, Konnerth A, Marie H, Haass C (2015) eta-Secretase processing of APP inhibits neuronal activity in the hippocampus. *Nature* 526 :443-7.

Bachhuber T, Katzmarski N, McCarter JF, Loreth D, Tahirovic S, Kamp F, Abou-Ajram C, Nuscher B, Serrano-Pozo A, Muller A, Prinz M, Steiner H, Hyman BT, Haass C, Meyer-Luehmann M (2015) Inhibition of amyloid-beta plaque formation by alpha-synuclein. *Nature medicine* 21: 802-807.

Kleinberger G., Yamanishi Y., Suárez-Calvet M., Czirr E., Lohmann E., Cuyvers E., Struyfs H., Pettkus N., Wenninger-Weinzierl A., Mazaheri F., Tahirovic S., Lleó A., Alcolea D., Fortea J., Willem M., Lammich S., Molinuevo J. L., Sanchez-Valle R., Antonell A., Ramirez A., Heneka M., Sleegers K., van der Zee J., Martin J.-J., Engelborghs S., Demirtas-Tatlıdide A., Zetterberg H., Van Broeckhoven C., Gurvit H., Wyss-Coray T., Hardy J., Colonna M. & Haass C. (2014) TREM2 mutations linked to neurodegeneration impair cell surface transport and phagocytosis. *Science Translational Medicine*, 6, 1-29.

Fleck D, van Bebber F, Colombo A, Galante C, Schwenk BM, Rabe L, Hampel H, Novak B, Kremmer E, Tahirovic S, Edbauer D, Lichtenthaler SF, Schmid B, Willem M, Haass C. (2013). Dual cleavage of Neuregulin I type III by BACE1 and ADAM17 liberates its EGF-like domain and allows paracrine signaling. *J Neurosci.*, 33, 7856-69

Schmid B, Hruscha A, Hogl S, Banzhaf-Strathmann J, Strecker K, van der Zee J, Teucke M, Eimer S, Hegermann J, Kittelmann M, Kremmer E, Cruts M, Solchenberger B, Hasenkamp L, van Bebber F, Van Broeckhoven C, Edbauer D, Lichtenthaler SF, Haass C. (2013). Loss of ALS-associated TDP-43 in zebrafish causes muscle degeneration, vascular dysfunction, and reduced motor neuron axon outgrowth. *Proc Natl Acad Sci U S A.*, 110, 4986-91

Mori K, Weng SM, Arzberger T, May S, Rentzsch K, Kremmer E, Schmid B, Kretzschmar HA, Cruts M, Van Broeckhoven C, Haass C, Edbauer D. (2013) The C9orf72 GGGGCC repeat is translated into aggregating dipeptide-repeat proteins in FTLN/ALS. *Science.* 15, 1335-8.

Dormann, D., Madl, T., Valori, C.V., Bentmann, E., Tahirovic, S., Abou-Ajram, C., Kremmer, K., Ansorge, O., Mackenzie, I.R.A., Neumann, M., Haass, C. (2012). Arginine methylation next to the PY-NLS modulates Transportin binding and nuclear import of FUS. *EMBO J.*, 31, 4258-4275.

Capell, A., Liebscher, S., Fellerer, K., Brouwers, N., Willem, M., Lammich, S., Gijssels, I., Bittner, T., Carlson, A.M., Sasse, F., Kunze, B., Steinmetz, H., Jansen, R., Dormann, D., Sleegers, K., Cruts, M., Herms, J., Van Broeckhoven, C., Haass, C. (2011). Rescue of Progranulin Deficiency Associated with Frontotemporal Lobar Degeneration by Alkalinizing Reagents and Inhibition of Vacuolar ATPase. *J. Neurosci.*, 31, 1885 - 1894.

Kamp, F., Exner N., Lutz A.K., Wender N., Hegermann J., Brunner, B., Nuscher, B., Bartels, T., Giese, A. Beyer, K., Eimer, S., Winklhofer, K.F., Haass, C. (2010). Inhibition of mitochondrial fusion by α -synuclein is rescued by PINK1, Parkin and DJ-1. *EMBO J.*, 29, 3571 - 3589.

Dormann, D, Rodde, R, Edbauer, D, Bentmann, E, Fischer, I, Hruscha, A, Than ME, Mackenzie I RA, Capell A, Schmid S, Neumann M, Haass, C. (2010). ALS-associated *fused in sarcoma (FUS)* mutations disrupt Transportin mediated nuclear import. *EMBO J.*, 29, 2841-2857.

Fukumori, A., Fluhrer, R., Steiner, H., and Haass, C. (2010). Three-amino acid spacing of presenilin endoproteolysis suggests a general stepwise cleavage of γ -secretase-mediated intramembrane proteolysis. *J. Neuroscience* 30, 7853-7862.

Paquet D, Bhat R, Sydow A, Mandelkow EM, Berg S, Hellberg S, Falting J, Distel M, Koster RW, Schmid B, Haass C. (2009) Gal4-UAS based transgenic expression of amyloidogenic proteins allows

early detection of disease specific neuropathology in zebrafish. *J. Clinical Investigation*, 119, 1382 - 1395.

Exner, N., Treske, B., Paquet, D., Holmstrom, K., Schiesling, C., Gispert, S., Carballo-Carbajal, I., Berg, D., Hoepken, H. H., Gasser, T., Krüger R., Winklhofer K.F., Vogel, F., Reichert, A.S., Auburger, G., Kahle, P.J., Schmid, B., and Haass, C. (2007). Loss-of-function of human PINK1 results in mitochondrial pathology and can be rescued by parkin. *J Neurosci* 27, 12413-12418.

Kaether, C., Scheuermann, J., Fassler, M., Zilow, S., Shirotani, K., Valkova, C., Novak, B., Kacmar, S., Steiner, H. and Haass, C. (2007) Endoplasmic reticulum retention of the gamma-secretase complex component Pen2 by Rer1. *EMBO Rep* 8, 743-8.

Willem, M., Garratt, A.N., Novak, B., Citron, M., Kaufmann, S., Rittger, A., DeStrooper, B., Saftig, P., Birchmeier, C. and Haass, C. (2006) Control of peripheral nerve myelination by the beta-secretase BACE1. *Science* 314, 664-6.

Fluhrer, R., Grammer, G., Israel, L., Condrón, M.M., Haffner, C., Friedmann, E., Bohland, C., Imhof, A., Martoglio, B., Teplow, D.B. and Haass, C. (2006) A gamma-secretase-like intramembrane cleavage of TNFalpha by the GxGD aspartyl protease SPPL2b. *Nat Cell Biol* 8, 894-6.

Kaether, C., Capell, A., Edbauer, D., Winkler, E., Novak, B., Steiner, H. and Haass, C. (2004) The presenilin C-terminus is required for ER-retention, nicastrin-binding and gamma-secretase activity. *EMBO J* 23, 4738-48.

Haffner, C., Frauli, M., Topp, S., Irmeler, M., Hofmann, K., Regula, J.T., Bally-Cuif, L. and Haass, C. (2004) Nicalin and its binding partner Nomo are novel Nodal signaling antagonists. *EMBO J* 23, 3041-50.

Lammich, S., Schobel, S., Zimmer, A.K., Lichtenthaler, S.F. and Haass, C. (2004) Expression of the Alzheimer protease BACE1 is suppressed via its 5'-untranslated region. *EMBO Rep* 5, 620-5.

Edbauer, D., Winkler, E., Regula, J.T., Pesold, B., Steiner, H. and Haass, C. (2003) Reconstitution of gamma-secretase activity. *Nat Cell Biol* 5, 486-8.

Okochi, M., Steiner, H., Fukumori, A., Tanii, H., Tomita, T., Tanaka, T., Iwatsubo, T., Kudo, T., Takeda, M. and Haass, C. (2002) Presenilins mediate a dual intramembraneous gamma-secretase cleavage of Notch-1. *EMBO J* 21, 5408-16.

Kaether, C., Lammich, S., Edbauer, D., Ertl, M., Rietdorf, J., Capell, A., Steiner, H. and Haass, C. (2002) Presenilin-1 affects trafficking and processing of betaAPP and is targeted in a complex with nicastrin to the plasma membrane. *J Cell Biol* 158, 551-61.

Geling, A., Steiner, H., Willem, M., Bally-Cuif, L. and Haass, C. (2002) A gamma-secretase inhibitor blocks Notch signaling in vivo and causes a severe neurogenic phenotype in zebrafish. *EMBO Rep* 3, 688-94.

Kahle, P.J., Neumann, M., Ozmen, L., Muller, V., Jacobsen, H., Spooren, W., Fuss, B., Mallon, B., Macklin, W.B., Fujiwara, H., Hasegawa, M., Iwatsubo, T., Kretschmar, H.A. and Haass, C. (2002) Hyperphosphorylation and insolubility of alpha-synuclein in transgenic mouse oligodendrocytes. *EMBO Rep* 3, 583-8.

Sastre, M., Steiner, H., Fuchs, K., Capell, A., Multhaup, G., Condrón, M.M., Teplow, D.B. and Haass, C. (2001) Presenilin-dependent gamma-secretase processing of beta-amyloid precursor protein at a site corresponding to the S3 cleavage of Notch. *EMBO Rep* 2, 835-41.

Steiner, H., Kostka, M., Romig, H., Basset, G., Pesold, B., Hardy, J., Capell, A., Meyn, L., Grim, M.L., Baumeister, R., Fichtler, K. and Haass, C. (2000) Glycine 384 is required for presenilin-1 function and is conserved in bacterial polytopic aspartyl proteases. *Nat Cell Biol* 2, 848-51.

Capell, A., Steiner, H., Romig, H., Keck, S., Baader, M., Grim, M.G., Baumeister, R. and Haass, C. (2000) Presenilin-1 differentially facilitates endoproteolysis of the beta-amyloid precursor protein and Notch. *Nat Cell Biol* 2, 205-11.

Walter, J., Schindzielorz, A., Grunberg, J. and Haass, C. (1999) Phosphorylation of presenilin-2 regulates its cleavage by caspases and retards progression of apoptosis. *Proc Natl Acad Sci U S A* 96, 1391-6.

Walter, J., Grunberg, J., Capell, A., Pesold, B., Schindzielorz, A., Citron, M., Mendla, K., George-Hyslop, P.S., Multhaup, G., Selkoe, D.J. and Haass, C. (1997) Proteolytic processing of the Alzheimer disease-associated presenilin-1 generates an in vivo substrate for protein kinase C. *Proc Natl Acad Sci U S A* 94, 5349-54.

Haass, C., Lemere, C.A., Capell, A., Citron, M., Seubert, P., Schenk, D., Lannfelt, L. and Selkoe, D.J. (1995) The Swedish mutation causes early-onset Alzheimer's disease by beta-secretase cleavage within the secretory pathway. *Nat Med* 1, 1291-6.

Haass, C., Koo, E.H., Capell, A., Teplow, D.B. and Selkoe, D.J. (1995) Polarized sorting of beta-amyloid precursor protein and its proteolytic products in MDCK cells is regulated by two independent signals. *J Cell Biol* 128, 537-47.

Haass, C., Koo, E.H., Teplow, D.B. and Selkoe, D.J. (1994) Polarized secretion of beta-amyloid precursor protein and amyloid beta-peptide in MDCK cells. *Proc Natl Acad Sci U S A* 91, 1564-8.

Haass, C., Schlossmacher, M.G., Hung, A.Y., Vigo-Pelfrey, C., Mellon, A., Ostaszewski, B.L., Lieberburg, I., Koo, E.H., Schenk, D., Teplow, D.B., and Selkoe, D.J. (1992) Amyloid beta-peptide is produced by cultured cells during normal metabolism. *Nature* 359, 322-5.

Haass, C., Koo, E.H., Mellon, A., Hung, A.Y. and Selkoe, D.J. (1992) Targeting of cell-surface beta-amyloid precursor protein to lysosomes: alternative processing into amyloid-bearing fragments. *Nature* 357, 500-3.

Haass, C., Hung, A.Y. and Selkoe, D.J. (1991) Processing of beta-amyloid precursor protein in microglia and astrocytes favors an internal localization over constitutive secretion. *J Neurosci* 11, 3783-93.

Haass, C., Pesold-Hurt, B., Multhaup, G., Beyreuther, K. and Kloetzel, P.M. (1989) The PROS-35 gene encodes the 35 kd protein subunit of *Drosophila melanogaster* proteasome. *EMBO J* 8, 2373-9.

Falkenburg, P.E., Haass, C., Kloetzel, P.M., Niedel, B., Kopp, F., Kuehn, L. and Dahlmann, B. (1988) *Drosophila* small cytoplasmic 19S ribonucleoprotein is homologous to the rat multicatalytic proteinase. *Nature* 331, 190-2.

Selected Review Articles

Dormann D. and Haass C. (2013) Fused in sarcoma (FUS): An oncogene goes awry in neurodegeneration. *Mol. Cell Neurosci*, (Epub ahead of print)

Dormann, D. & Haass, C. (2011). TDP-43 and FUS - a nuclear affair. *Trends in Neuroscience*, 7, 339-348.

St George-Hyslop, P., and Haass, C. (2008). Regulatory RNA goes awry in Alzheimer's disease. *Nat. Med.* 14, 711-712.

Winklhofer, K.F., Tatzelt, J., and Haass, C. (2008). The two faces of protein misfolding: gain- and loss-of-function in neurodegenerative diseases. *EMBO J.* 27, 336-349.

Haass, C. and Selkoe, D.J. (2007) Soluble protein oligomers in neurodegeneration: lessons from the Alzheimer's amyloid beta-peptide. *Nat Rev Mol Cell Biol* **8**, 101-12.

Haass, C. (2004) Take five--BACE and the gamma-secretase quartet conduct Alzheimer's amyloid beta-peptide generation. *EMBO J* **23**, 483-8.

Kaether, C. and Haass, C. (2004) A lipid boundary separates APP and secretases and limits amyloid beta-peptide generation. *J Cell Biol* **167**, 809-12.

Aguzzi, A. and Haass, C. (2003) Games played by rogue proteins in prion disorders and Alzheimer's disease. *Science* **302**, 814-8.

Haass, C. and Steiner, H. (2002) Alzheimer disease gamma-secretase: a complex story of GxGD-type presenilin proteases. *Trends Cell Biol* **12**, 556-62.

Haass, C. (2002) New hope for Alzheimer disease vaccine. *Nat Med* **8**, 1195-6.

Haass, C. and Steiner, H. (2001) Protofibrils, the unifying toxic molecule of neurodegenerative disorders? *Nat Neurosci* **4**, 859-60.

Haass, C. and Kahle, P.J. (2001) Neuroscience. Parkin and its substrates. *Science* **293**, 224-5.

Kahle, P.J., Leimer, U. and Haass, C. (2000) Does failure of parkin-mediated ubiquitination cause juvenile parkinsonism? *Trends Biochem Sci* **25**, 524-7.

Haass, C. and Kahle, P.J. (2000) Parkinson's pathology in a fly. *Nature* **404**, 341, 343.

Haass, C. and De Strooper, B. (1999) The presenilins in Alzheimer's disease--proteolysis holds the key. *Science* **286**, 916-9.

Haass, C. and Selkoe, D.J. (1998) Alzheimer's disease. A technical KO of amyloid-beta peptide. *Nature* **391**, 339-40.

Haass, C. (1997) Presenilins: genes for life and death. *Neuron* **18**, 687-90.

Haass, C. (1996) Presenile because of presenilin: the presenilin genes and early onset Alzheimer's disease. *Curr Opin Neurol* **9**, 254-9.

Haass, C. and Selkoe, D.J. (1993) Cellular processing of beta-amyloid precursor protein and the genesis of amyloid beta-peptide. *Cell* **75**, 1039-42.