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Research

- 2021 – present Professor of Molecular Biology, Max Perutz Labs, Medical University of Vienna
- 2017 – 2021 Associate Professor, Max Perutz Labs, Medical University of Vienna
- 2012 – 2017 Junior Group Leader, Max Perutz Labs, Medical University of Vienna
- 2005 – 2011 Postdoctoral Fellow, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK/NIH)
Advisor: Dr. James H. Hurley
- 2001 – 2005 PhD student, MRC Laboratory of Molecular Biology (LMB), Cambridge, U.K.
Advisor: Dr. Jan Löwe

Education

- 2001 – 2005 PhD, University of Cambridge. Advisor: Jan Löwe, Structural Studies Division
- 1998 – 2001 BSc (Hons) Biochemistry with Medical Biochemistry, University of Bristol, U.K. (First Class Honours)

Funding

- 2023 – 2027 Austrian Research Fund (FWF) Project (P 36212)
'Phosphoinositide-dependent kinase 1: master growth regulator.'
- 2020 – 2023 Austrian Research Fund (FWF) Project (P 33066)
'PI3K signaling – navigating upstream and downstream of Akt.'
- 2019 – 2021 Austrian Academy of Sciences DOC PhD Fellowship to K. Siess.
- 2017 – 2020 Austrian Research Fund (FWF) Project (P 30584)
'Structure, Function, and Regulation of Protein Kinase D.'

- 2017 – 2020 Austrian Research Fund (FWF) Hertha Firnberg Postdoctoral Fellowship to Dr. Linda Trübestein (T 915).
- 2017 – 2020 Austrian Research Fund (FWF) Doctoral Program “Signaling Mechanisms in Cellular Homeostasis”.
- 2015 – 2018 Austrian Research Fund (FWF) Project (P 28135)
‘Lipid-activated kinases in cell shape and motility.’
- 2017 – 2017 University of Vienna Thesis Completion Fellowship to I. Lučić.
- 2015 – 2017 Boehringer Ingelheim Fonds (BIF) PhD Fellowship to D. Elsner.
- 2014 – 2016 Austrian Academy of Sciences DOC PhD Fellowship to F. von Raußendorf.

Honours and Awards

- 2016 F1000Prime Faculty Member: Cell Signaling & Trafficking Structures Section
- 2006-2012 NIDDK Nancy Nossal Fellowship (National Institutes of Health (NIH), U.S.A.)
- 2006-2008 EMBO Long Term Fellowship

Invited Talks

- 2023 First Focused Meeting on Molecular Mechanisms of PDK1/Akt. Barcelona, Spain.
- 2022 88th Harden Conference: ‘Beyond catalysis: kinases and pseudokinases 2022’, Chesford Grange, U.K.
- 2022 EMBO Workshop: Cancer Cell Signaling, Cavtat, Croatia
- 2022 Max Perutz Exhibition: Breathing at High Altitude. ‘Max Perutz: a not so quiet life.’
- 2022 Max Perutz Exhibition: Breathing at High Altitude. ‘Standing on the shoulders of giants – the legacy of Max Perutz.’
- 2022 FASEB conference ‘Protein Kinases and Protein Phosphorylation’, Nova Scotia, CA
- 2021 OEGMBT 13th Annual Meeting: ‘From Molecular Machines to Translational Medicine’
- 2019 FASEB conference ‘Protein Kinases and Protein Phosphorylation’, Palm Springs, USA
- 2018 International Workshop on Biological Membranes, Helsinki, Finland
- 2018 FASEB conference ‘Phospholipids: Dynamic Lipid Signaling in Health and Disease’, Steamboat Springs, CO USA
- 2017 FASEB conference ‘Protein Kinases and Protein Phosphorylation’, Cambridge, UK
- 2017 Keystone Symposium ‘PI3K Pathways in Immunology, Growth Disorders and Cancer’, Santa Fe, New Mexico, USA
- 2017 Biomolecules and Nanostructures 6, Podlesice, Poland
- 2015 FASEB conference ‘Protein Kinases and Protein Phosphorylation’, Itasca, IL USA

Teaching/Mentoring Experience

- 2012 – Supervision of five Masters students and four PhD students
- 2017 – Biophysical Chemistry of Macromolecules
- 2015 – Lecture Series: Advanced Biophysical Methods
- 2015 – Lecture Series: Molecular Medicine I
- 2014 – Lecture Series: Methods in Molecular Biology and Biochemistry
- 2013 – Practical course: Molecular Biophysics (formerly Spectroscopic Methods)
- 2013 – Introductory Course in Cell Signaling
- 2012 VBC PhD Lecture Series: ‘Lipid-Activated Signal Transduction’
- 2010 Mentor, Summer Internship Program, NIH, U.S.A.
- 2003 – 2005 Undergraduate Tutor, Corpus Christi College, University of Cambridge, U.K.

Commissions of Trust

- 2021 – present Curriculum Director, MSc Molecular Precision Medicine (joint programme of Medical University of Vienna and University of Vienna)
<https://www.meduniwien.ac.at/web/en/studies-further-education/the-molecular-precision-medicine-masters-programme/>
- 2020 – present Vice-Dean of the Max Perutz Labs
Deputy Head of the Center for Medical Biochemistry, Medical University of Vienna
Deputy Doctoral Studies Programme Leader, Vienna BioCenter PhD Programme
- 2018 – present Tenure Track hiring committees, University of Vienna and Medical University of Vienna
- 2018 Vienna Biocenter PhD Awards committee
- 2016 – Mass Spectrometry User Committee, MFPL

Peer Review Activities

- F1000 Faculty Opinions Faculty Member: Cell Signaling & Trafficking Structures Section
- Journals Acta Cryst D; Biochemistry; Cell; Chemical Reviews; Nature Communications; Nature Structural and Molecular Biology; PLoS Biology; PNAS; Science; Science Signaling; Scientific Reports.
- Grant review Agence Nationale de la Recherche (France).

Publications

- Reinhardt, R. and **Leonard, T.A.** (2023) A critical evaluation of protein kinase regulation by activation

loop autophosphorylation. *eLife* Jul 20;12:e88210. doi: 10.7554/eLife.88210.

Leonard, T.A., Loose, M. and Martens, S. (2023) The membrane surface as a platform that organizes cellular and biochemical processes. *Dev Cell* Jun 28;S1534-5807(23)00274-5. doi: 10.1016/j.devcel.2023.06.001.

Reinhardt, R., Hirzel, K., Link, G., Eisler, S.A., Haegele, T., Parson, M.A.H., Burke, J.E., Hausser, A., **Leonard, T.A.** (2023) PKD autoinhibition in *trans* regulates activation loop autophosphorylation in *cis*. *Proceedings of the National Academy of Sciences* Feb 14;120(7):e2212909120. (doi: 10.1073/pnas.2212909120).

Truebestein, L., Antonioli, S., Waltenberger, E., Gehin, C., Gavin, A., **Leonard, T.A.** (2023) Structure and regulation of the myotonic dystrophy kinase-related Cdc42-binding kinase. *Structure* Feb 23:S0969-2126(23)00036-9. (doi: 10.1016/j.str.2023.02.002).

Thibodeau, M.C., Harris, N.J., Jenkins, M.L., Parson, M.A.H., Evans, J.T., Scott, M.K., Shaw, A.L., Pokorny, D., **Leonard, T.A.**, Burke J.E. (2023) Molecular basis for the recruitment of the Rab effector protein WDR44 by the GTPase Rab11. *J Biol Chem.* Jan;299(1):102764. (doi: 10.1016/j.jbc.2022.102764).

Shaw, A.L., Parson, M.A.H., Truebestein, L., Jenkins, M.L., **Leonard, T.A.**, Burke, J.E. (2023) ATP-competitive and allosteric inhibitors induce differential conformational changes at the autoinhibitory interface of Akt. *Structure* Mar 2;31(3):343-354.e3. (doi: 10.1016/j.str.2023.01.007).


Levina, A., Fleming, K.D., Burke, J.E.B., **Leonard, T.A.** (2022) Activation of the essential kinase PDK1 by phosphoinositide-driven trans-autophosphorylation. *Nature Communications.* Apr 6;13(1):1874. doi: 10.1038/s41467-022-29368-4.

Truebestein, L., Hornegger, H., Anrather, D., Hartl, M., Fleming, K.D., Stariha, J.T.B., Pardon, E., Steyaert, J., Burke, J.E., and **Leonard, T.A.** (2021) Structure of autoinhibited Akt1 reveals mechanism of PIP₃-mediated activation. *Proceedings of the National Academy of Sciences.* Aug 17;118(33):e2101496118. (doi: 10.1073/pnas.2101496118).

Pokorny, D., Truebestein, L., Fleming, K.D., Burke, J.E., and **Leonard, T.A.** (2021) *In vitro* reconstitution of Sgk3 activation by phosphatidylinositol 3-phosphate. *J Biol Chem.* Jun 25;100919. (doi: 10.1016/j.jbc.2021.100919).

Reinhardt, R., Truebestein, L., Schmidt, H.A., and **Leonard, T.A.** (2020) It takes two to tango: activation of protein kinase D by dimerization. *Bioessays.* Jan 29:e1900222. (doi: 10.1002/bies.201900222).

Elsner, D.J., Siess, K.M., Gossenreiter, T., Hartl, M., **Leonard, T.A.** (2019) A ubiquitin-like domain controls protein kinase D dimerization and activation by trans-autophosphorylation. *J Biol Chem.* Aug 12. pii: jbc.RA119.008713. (doi: 10.1074/jbc.RA119.008713).

- Siess, K.M. and **Leonard, T.A.** (2019) Lipid-dependent Akt-ivity: where, when, and how. *Biochem. Soc. Trans.* (doi: 10.1042/BST20190013).
- Tripathy, R., Leca, I., van Dijk, T., Weiss, J., van Bon, B.W., Sergaki, M.C., Gstrein, T., Breuss, M., Tian, G., Bahi-Buisson, N., Paciorkowski, A.R., Pagnamenta, A.T., Wenninger-Weinzierl, A., Martinez-Reza, M.F., Landler, L., Lise, S., Taylor, J.C., Terrone, G., Vitiello, G., Del Giudice, E., Brunetti-Pierri, N., D'Amico, A., Reymond, A., Voisin, N., Bernstein, J.A., Farrelly, E., Kini, U., **Leonard, T.A.**, Valence, S., Burglen, L., Armstrong, L., Hiatt, S.M., Cooper, G.M., Aldinger, K.A., Dobyns, W.B., Mirzaa, G., Pierson, T.M., Baas, F., Chelly, J., Cowan, N.J., Keays, D.A. (2018) Mutations in MAST1 Cause Mega-Corpus-Callosum Syndrome with Cerebellar Hypoplasia and Cortical Malformations. *Neuron pii: S0896-6273(18)30952-8.* (doi: 10.1016/j.neuron.2018.10.044).
- Leonard, T.A.** (2018) Reply to Agarwal: Activity against nuclear substrates is not necessarily mediated by nuclear Akt. *Proceedings of the National Academy of Sciences* 115(27):E6101-E6102. (doi: 10.1073/pnas.1808882115).
- Lučić, I., Rathinaswamy, M.K., Truebestein, L., Hamelin, D., Burke, J.E., **Leonard, T.A.** (2018) Conformational sampling of membranes by Akt controls its activation and inactivation. *Proceedings of the National Academy of Sciences* 115(17):E3940-E3949. (doi: 10.1073/pnas.1716109115).
- von Raußendorf, F., de Ruiter, A., **Leonard, T.A.** (2017) A switch in nucleotide affinity governs activation of the Src and Tec family kinases. *Scientific Reports* 7(1):17405 (doi: 10.1038/s41598-017-17703-5).
- ¹Ebner, M., ¹Lučić, I., ***Leonard, T.A.**, *Yudushkin, I. (2017) PI(3,4,5)P₃ restricts Akt activity to cellular membranes. *Molecular Cell* 65(3):416-431 (doi: 10.1016/j.molcel.2016.12.028).
- ¹Co-first authors; *Co-corresponding authors.
- Truebestein, L., **Leonard, T.A.** (2016) Coiled-coils: The long and short of it. *BioEssays* 38:903-916 (doi: 10.1002/bies.201600062). Review.
- Truebestein, L., Elsner, D.J., **Leonard, T.A.** (2016). Made to measure – keeping Rho kinase at a distance. *Small GTPases* 7(2):82-92 (doi: 10.1080/21541248.2016.1173770). Review.
- Truebestein, L., Elsner, D.J., Fuchs, E., **Leonard, T.A.** (2015). A molecular ruler regulates cytoskeletal remodelling by the Rho kinases. *Nature Communications* 6:10029 (doi: 10.1038/10029).
- F1000 Prime Recommended.** 
- Lučić, I., Truebestein, L., **Leonard, T.A.** (2015). Novel features of DAG-activated PKC isozymes reveal a conserved 3-D architecture. *Journal of Molecular Biology* 428(1):121-41 (doi: 10.1016/j.jmb.2015.11.001).
- Gutierrez-Uzquiza, A., Colon-Gonzalez, F., **Leonard, T.A.**, Canagarajah, B.J., Wang, H., Mayer, B., Hurley,

J.H., Kazanietz, M.G. (2013). Coordinated activation of the Rac-GAP β 2-chimaerin by an atypical proline-rich domain and diacylglycerol. *Nature Communications* 4:1849 (doi: 10.1038/ncomms2834).

Yang, H., Tong, J., **Leonard, T.A.**, Im Y.J. (2013). Structural determinants for phosphatidylinositol recognition by Sfh3 and substrate-induced dimer-monomer transition during lipid transfer cycles. *FEBS Lett.* 5;587(11):1610-6 (doi: 10.1016/j.febslet.2013.04.009).

Leonard, T.A. C2 domain proteins. *Encyclopedia of Metalloproteins*. (2013). (doi 10.1007/978-1-4614-1533-6). Book chapter.

Leonard, T.A., Hurley, J.H. (2011). Regulation of protein kinases by lipids. *Curr Opin Struct Biol* 21, 785-791. Review.

Leonard, T.A., Rozycki, B., Saidi, L.F., Hummer, G., Hurley, J.H. (2011). Crystal structure and allosteric activation of Protein Kinase C β II. *Cell* 144 (1), 55-66.

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(Comment on: Kazanietz, M.G., Lemmon, M.A. (2011). Protein Kinase C regulation: C1 meets C-tail. *Structure* 19 (2) 144-146).

Wu, Y., Sommers, J.A., Suhasini, A.N., **Leonard, T.A.**, Deakyne, J.S., Mazin, A.V., Shin-ya, K., Kitao, H., Brosh, R.M. (2010). Fanconi Anemia Group J Mutation Abolishes its DNA Repair Function by Uncoupling DNA Translocation from Helicase Activity or Disruption of Protein-DNA Complexes. *Blood* 116(19) 3780-91.

Oliva M.A., Halbedel S., Freund S.M., Dutow P., **Leonard T.A.**, Veprintsev D.B., Hamoen L.W., Löwe J. (2010). Features critical for membrane binding revealed by DivIVA crystal structure. *EMBO J.* 29(12):1988-2001

Leonard, T.A., Hurley, J.H. (2007). Two Kinase Family Dramas. *Cell* 129 (6), 1037-1038. Preview.

Leonard, T.A., Møller-Jensen, J., Löwe, J. (2005). Towards understanding the molecular basis of bacterial DNA segregation. *Philos Trans R Soc Lond B Biol Sci.* 360 (1455), 523-35. Review.

Leonard, T.A., Butler, P.J.G., Löwe, J. (2005). Bacterial chromosome segregation: Structure and DNA binding of the Soj dimer – a conserved biological switch. *EMBO J.* 24(2), 270-82.

Leonard, T.A., Butler, P.J.G., Löwe, J. (2004). Structural analysis of the chromosome segregation protein Spo0J from *Thermus thermophilus*. *Molecular Microbiology* 53(2), 419-432.