

Xaver König

Current address

Center for Physiology and Pharmacology, Dept. Neurophysiology and –
pharmacology, Medical University of Vienna, Schwarzschanerstrasse 17,
1090 Vienna, Austria

Personal Data

Date of birth 08.03.1979
Place of birth Vienna, Austria
Nationality Austria

Career history

- 2018 – ... **Entwicklungsvereinbarung** Medical University of Vienna, Austria (equivalent to **Assistant professor with tenure-track**)
- 2017 – 2018 **Postdoctoral Research Fellow** at the Department for Neurophysiology and –
–pharmacology, Medical University of Vienna, Austria
- 2015 – 2017 **Postdoctoral Research Fellow** at the Muscle Research Laboratory, School of
Biomedical Sciences, Queensland University, Brisbane, Australia
- 2012 – 2015 **Postdoctoral Research Fellow** at the Department for Neurophysiology and
–pharmacology, Medical University of Vienna, Austria
- 2007 – 2012 **Ph.D., Medical University of Vienna, Austria**
Thematic program: "Molecular Signal Transduction"
Thesis title: "*Impaired ion channel function in Duchenne muscular dystrophy*",
Supervisor: Prof. Karlheinz Hilber
- 1998 – 2006 **M.S., Physics, Technical University of Vienna, Austria**
At the Institute of Atomic and Subatomic Physics
Thesis title: "*Investigation of the phase transition in the model of topological
fermions*", Supervisor: Prof. Manfred Faber

Teaching

- 2015 – 2017 within BIOM2011, University of Queensland
– Practical courses in physiology
- 2013 – ... within curriculum N202: human medicine, Medical University of Vienna
– block 2, Lecture: Muscle physiology
– block 4, Lecture: Functional systems and biological regulation
Seminar and Practical course: Neurophysiology
– block 18, Practical course: skin and sensory organs
– block 19, Practical course: brain and nervous system

Student supervision

- 2018 - ... Nicholas Hächl (Diploma student)
- 2015 – 2017 Co-supervision of honor (Joshua Haywood), master (Zoe Macourt), and PhD students
(Rocky Choi)

2007 – 2015 Co-supervision of master (Markus Mille, Michael Kovar) and PhD students (Lena Rubi, Agnes Mike)

Main research areas

- Skeletal and cardiac muscle physiology in the context of muscular dystrophies
- Pharmacology of ion channels, in particular cardiac ion channels
- Calcium handling in skeletal muscle
- Store-operated Calcium entry in skeletal muscle

Scientific talks and awards

“Ion channel impairments in dystrophic cardiomyocytes“

15th Scientific Symposium of APHAR, Graz, 2009

Prize for best oral communication

“Altered sodium channel function in dystrophin/utrophin-deficient cardiomyocytes”

16th Scientific Symposium of APHAR, Vienna, 2010

Prize for best oral communication

“The indole alkaloid ibogaine and its mechanism of $K_v11.1$ (hERG) channel block”

19th Scientific Symposium of APHAR, Vienna, 2013

“Real time imaging of trans-sarcolemma Ca^{2+} -fluxes in mammalian skeletal muscle”

AuPS/ASB joint meeting, Adelaide, 2016

“Towards the role of store-operated Ca^{2+} entry in skeletal muscle”, FEPS meeting, Vienna, 2017

Nomination for „österreichischer Staatspreis Patent“ (category „Spezialpreis Hedy-Lamarr“) 2016:
“Pyridine und Pyrimidine als cardiogene Wirkstoffe“

Invention notifications and patents

“Composition for the treatment of cystic fibrosis”

PCT: WO2011015630, Co-inventors: Freissmuth M. & Gloeckel C.

“Substituted pyridines and pyrimidines for the production of cardiomyocyte-like cells”

PCT: WO2011079343, Co-inventors: Mihovilovic M., Schnuerch M., Koley M. & Hilber K.

„Triazin-Derivate als Differenzierungsbeschleuniger“

AT 511441, Co-inventors: Mihovilovic M., Schnuerch M., Hilber K., Linder T. & Mike A.

Memberships

Österreichische Pharmakologische Gesellschaft (APHAR)

Österreichische Biophysikalische Gesellschaft (OeBG)

Australian Physiological Society (AuPS)

Third-party funding

„Cardiogenic agents“, AWS (Austria Wirtschaftsservice) PRIZE project: Z090391, 38.000 EUR

„Defining the Role of Store-operated Calcium Entry in Dystrophic Skeletal Muscle“, Österreichische Muskelforschung, 17.320 EUR

„Store-operated Calcium Entry in Skeletal Muscle“, Fonds zur Förderung der wissenschaftlichen Forschung (FWF), 330.000EUR

Reviewer for

Journal of Molecular and Cellular Cardiology, Neuropharmacology, British Journal of Pharmacology, Natural product research, Journal of psychoactive drugs

10 most relevant publications

1) **Koenig X.**, Dysek S., Kimbacher S., Mike AK., Cervenka R., Lukacs P., Nagl K., Dang XB., Todt H., Bittner RE., Hilber K. (2011). Voltage-gated ion channel dysfunction precedes cardiomyopathy development in the dystrophic heart. *PLoS One* **6(5)**: p.e20300.

2) **Koenig X.**, Kovar M., Rubi L., Mike A., Lukacs P., Gawali V., Todt H., Hilber K. & Sandtner W. (2013) Anti-addiction drug ibogaine inhibits cardiac ion channels: a study to assess the drug's proarrhythmic potential. *Toxicology and Applied Pharmacology*. **273(2)**: 259-68. doi: 10.1016/j.taap.2013.05.012

3) Thurner P., Stary-Weinzinger A., Gafar H., Zezula J., Hilber K., Boehm S., Sandtner W and **Koenig X.** (2014) Mechanism of hERG channel block by the psychoactive indole alkaloid ibogaine. *J Pharmacol Exp Ther*. **348(2)**: 346-58. doi: 10.1124/jpet.113.209643

4) **Koenig X.***, Rubi L.* , Obermair G., Cervenka R., Dang X., Lukacs P., Kummer S., Bittner R., Kubista H., Todt H., and Hilber K. (2014) Enhanced currents through L-type calcium channels in cardiomyocytes disturb the electrophysiology of the dystrophic heart. *Am J Physiol Heart Circ Physiol*. **306(4)**: H564-73. doi: 10.1152/ajpheart.00441.2013. * **shared first author**

5) **Koenig X.***, Kovar M.* , Boehm S., Sandtner W., Hilber K. (2014). Anti-addiction drug ibogaine inhibits hERG channels: a cardiac arrhythmia risk! *Addict Biol*. **19(2)**: 237-9, doi: 10.1111/j.1369-1600.2012.00447.x. * **shared first author**

6) Treven M.* , **Koenig X.***, Assadpour E., Gantumur E., Meyer A., Hilber K., Boehm S., and Kubista H. (2015) The anticonvulsant retigabine is a subtype selective modulator of GABA-A receptors. *Epilepsia*. **56(4)**: 647-57. * **shared first author**

7) Klinger F., Bajric M., Assadpour E., Dorostkar MM., Khan D., Pollak DD., Kubista H., Boehm S, and **Koenig X.** (2015) δ -containing GABA-A receptors are preferred targets for the centrally acting analgesic flupirtine. *Br J Pharmacol*. doi: 10.1111/bph.13262.

8) Rubi L., Eckert D., Boehm S., Hilber K., and **Koenig X.** (2017) Anti-addiction Drug Ibogaine Prolongs the Action Potential in Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes. *Cardiovasc Toxicol*. **17(2)**: 215-218.

9) Choi R., **Koenig X.**, and Launikonis BS. (2017) Dantrolene requires Mg^{2+} to arrest malignant hyperthermia. *Proc Natl Acad Sci U S A*. doi: 10.1073/pnas.1619835114.

10) **Koenig X.**, Choi R., and Launikonis BS. (2018) Store-operated Ca^{2+} entry is activated by every action potential in skeletal muscle. *Communications Biology* **1**:31, doi: 10.1038/s42003-018-0033-7

Peer-reviewed Publications in the past 5 years

- 1) **Koenig X.**, Kovar M., Rubi L., Mike A., Lukacs P., Gawali V., Todt H., Hilber K. & Sandtner W. (2013) Anti-addiction drug ibogaine inhibits cardiac ion channels: a study to assess the drug's proarrhythmic potential. *Toxicology and Applied Pharmacology*. **273(2)**: 259-68. doi: 10.1016/j.taap.2013.05.012
- 2) Koley M., Mike AK., Heher P., **Koenig X.**, Schön M., Schnürch M., Hilber K., Weitzer G. and Mihovilovic MD. (2013) VUT-MK142: a new cardiomyogenic small molecule promoting the differentiation of pre-cardiac mesoderm into cardiomyocytes. *Med. Chem. Commun.* **4**: 1189–1195.
- 3) Thurner P., Stary-Weinzinger A., Gafar H., Zezula J., Hilber K., Boehm S., Sandtner W and **Koenig X.** (2014) Mechanism of hERG channel block by the psychoactive indole alkaloid ibogaine. *J Pharmacol Exp Ther.* **348(2)**: 346-58. doi: 10.1124/jpet.113.209643
- 4) Mike AK., **Koenig X.**, Koley M., Heher P., Wahl G., Rubi L, Schnürch M, Mihovilovic MD, Weitzer G and Hilber K. (2014) Small molecule cardiogenol C upregulates cardiac markers and induces cardiac functional properties in lineage-committed progenitor cells. *Cell Physiol Biochem.* **33(1)**: 205-21. doi: 10.1159/000356663.
- 5) Sandtner W., Schmid D., Schicker K., Gerstbrein K., **Koenig X.**, Mayer F., Boehm S., Freissmuth M., Sitte HH. (2014) A Quantitative Model of Amphetamine Action on the Serotonin Transporter. *Br J Pharmacol.* **171(4)**: 1007-18. doi: 10.1111/bph.12520.
- 6) **Koenig X.***, Rubi L.*, Obermair G., Cervenka R., Dang X., Lukacs P., Kummer S., Bittner R., Kubista H., Todt H., and Hilber K. (2014) Enhanced currents through L-type calcium channels in cardiomyocytes disturb the electrophysiology of the dystrophic heart. *Am J Physiol Heart Circ Physiol.* **306(4)**: H564-73. doi: 10.1152/ajpheart.00441.2013. * **shared first author**
- 7) **Koenig X.***, Kovar M.*, Boehm S., Sandtner W., Hilber K. (2014). Anti-addiction drug ibogaine inhibits hERG channels: a cardiac arrhythmia risk! *Addict Biol.* **19(2)**: 237-9, doi: 10.1111/j.1369-1600.2012.00447.x. * **shared first author**
- 8) Lukacs P., Gawali VS., Cervenka R., Ke S., **Koenig X.**, Rubi L., Zarrabi T., Hilber K., Stary-Weinzinger A., and Todt H. (2014) Exploring the structure of the voltage-gated Na⁺ channel by an engineered drug access pathway to the receptor site for local anesthetics. *J Biol Chem.* **289(31)**: 21770-81.
- 9) Schmid D., **Koenig X.**, Bulusu S., Schicker K., Freissmuth M., Sitte HH., and Sandtner W. (2015) The conservative view: is it necessary to implant a stent into the dopamine transporter? *Br J Pharmacol.* **172(19)**:4775-8.
- 10) Treven M.*, **Koenig X.***, Assadpour E., Gantumur E., Meyer A., Hilber K., Boehm S., and Kubista H. (2015) The anticonvulsant retigabine is a subtype selective modulator of GABA-A receptors. *Epilepsia.* **56(4)**: 647-57. * **shared first author**
- 11) **Koenig X.** and Hilber K. (2015) Review. Anti-addiction drug ibogaine and the heart: a delicate relation. *Molecules.* **20(2)**: 2208-28.
- 12) Rubi L., Gawali VS., Kubista H., Todt H., Hilber K.* and **Koenig X.** (2015) Proper voltage-dependent ion channel function in dysferlin-deficient cardiomyocytes. *Cell Physiol Biochem.* **36**: 1049-1058.

- 13) Hasenhuetl PS., Schicker K., **Koenig X.**, Yang L., Sarker S., Sucic S., Sitte HH, Freissmuth M, Sandtner W. (2015) Ligand Selectivity among the Dopamine and the Serotonin Transporter Specified by the Forward Binding Reaction. *Mol Pharmacol.* **88(1)**: 12-8.
- 14) Klinger F., Bajric M., Assadpour E., Dorostkar MM., Khan D., Pollak DD., Kubista H., Boehm S, and **Koenig X.** (2015) δ -containing GABA-A receptors are preferred targets for the centrally acting analgesic flupirtine. *Br J Pharmacol.* doi: 10.1111/bph.13262.
- 15) Gawali VS., Lukacs P., Cervenka R., **Koenig X.**, Rubi L., Hilber K., Sandtner W., and Todt H. (2015) Mechanism of Modification, by Lidocaine, of Fast and Slow Recovery from Inactivation of Voltage-Gated Na⁺ Channels. *Mol Pharmacol.* **88(5)**: 866-79.
- 16) Salzer I., Erdem FA., Chen W., Heo S., **Koenig X.**, Schicker K., Kubista H., Shapiro MS., Lubec G., Boehm S., and Yang J. (2017) Phosphorylation regulates the PIP2 sensitivity of voltage-gated Kv7.2 channels. Phosphorylation regulates the sensitivity of voltage-gated Kv7.2 channels towards phosphatidylinositol-4,5-bisphosphate. *J Physiol.* **595(3)**: 759-776.
- 17) Rubi L., **Koenig X.**, Kubista H., Todt H. & Hilber K. (2017) Decreased inward rectifier potassium current IK1 in dystrophin-deficient ventricular cardiomyocytes. *Channels* **25**: 1-8. doi: 10.1080/19336950.2016.1228498.
- 18) Rubi L., Eckert D., Boehm S., Hilber K., and **Koenig X.** (2017) Anti-addiction Drug Ibogaine Prolongs the Action Potential in Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes. *Cardiovasc Toxicol.* **17(2)**: 215-218.
- 19) Choi R., **Koenig X.**, and Launikonis BS. (2017) Dantrolene requires Mg²⁺ to arrest malignant hyperthermia. *Proc Natl Acad Sci U S A.* **114(18)**: 4811-4815, doi: 10.1073/pnas.1619835114.
- 20) Rubi L., Kovar M., Zebedin-Brandl E., **Koenig X.**, Dominguez-Rodriguez M., Todt H., Kubista H., Boehm S., and Hilber K. (2017) Modulation of the heart's electrical properties by the anticonvulsant drug retigabine. *Toxicol Appl Pharmacol.* **329**: 309-317. doi: 10.1016/j.taap.2017.06.018.
- 21) Mills RJ., Titmarsh DM., **Koenig X.**, Parker BL., Ryall JG., Quaipe-Ryan GA., Voges HK., Hodson MP., Ferguson C., Drowley L., Plowright AT., Needham EJ., Wang QD., Gregorevic P., Xin M., Thomas WG., Parton RG., Nielsen LK., Launikonis BS., James DE., Elliott DA., Porrello ER., and Hudson JE. (2017) Functional screening in human cardiac organoids reveals a metabolic mechanism for cardiomyocyte cell cycle arrest. *Proc Natl Acad Sci U S A.* **114(40)**: E8372-E8381, doi: 10.1073/pnas.1707316114.
- 22) Rubi L., Todt H., Kubista H., **Koenig X.***, and Hilber K. (2018) Calcium current properties in dystrophin-deficient ventricular cardiomyocytes from aged mdx mice. *Physiol Rep.*, doi: 10.14814/phy2.13567. * **corresponding author**
- 23) Cervenka R., Lukacs P., Gawali V., Ke S., **Koenig X.**, Rubi L., Zarrabi T., Hilber K., Sandtner W., Stary-Weinzinger A., and Todt H. (2018) Distinct modulation of inactivation by a residue in the pore domain of voltage-gated Na⁺ channels: mechanistic insights from recent crystal structures. *Sci Rep.* **8(1)**: 631. doi: 10.1038/s41598-017-18919-1.
- 24) **Koenig X.**, Choi R., and Launikonis BS. (2018) Store-operated Ca²⁺ entry is activated by every action potential in skeletal muscle. *Communications Biology* **1**:31, doi: 10.1038/s42003-018-0033-7.