



## Corrigendum to “Insight into the mechanism of cytotoxicity of membrane-permeant psoralenic Kv1.3 channel inhibitors by chemical dissection of a novel member of the family” [Redox Biol. 37 (2020 Sep 6) 101705–101721]

Roberta Peruzzo<sup>a</sup>, Andrea Mattarei<sup>b</sup>, Michele Azzolini<sup>c,1</sup>, Katrin Anne Becker-Flegler<sup>d</sup>, Matteo Romio<sup>e,2</sup>, Giovanni Rigoni<sup>a</sup>, Andrea Carrer<sup>a,c</sup>, Lucia Biasutto<sup>c,f</sup>, Sofia Parrasia<sup>c</sup>, Stephanie Kadow<sup>d</sup>, Antonella Managò<sup>a</sup>, Andrea Urbani<sup>a,c</sup>, Andrea Rossa<sup>e</sup>, Gianpietro Semenzato<sup>g</sup>, Maria Eugenia Soriano<sup>a</sup>, Livio Trentin<sup>g</sup>, Syed Ahmad<sup>h</sup>, Michael Edwards<sup>h</sup>, Erich Gulbins<sup>d</sup>, Cristina Paradisi<sup>e</sup>, Mario Zoratti<sup>e</sup>, Luigi Leanza<sup>a</sup>, Ildikò Szabò<sup>a,f,\*</sup>

<sup>a</sup> Department of Biology, University of Padua, Italy

<sup>b</sup> Department of Pharmaceutical and Pharmacological Sciences, University of Padua, Italy

<sup>c</sup> Department of Biomedical Sciences, University of Padua, Italy

<sup>d</sup> Department of Molecular Biology, University of Duisburg-Essen, Germany

<sup>e</sup> Department of Chemical Sciences, University of Padua, Italy

<sup>f</sup> CNR Institute of Neuroscience, Padua, Italy

<sup>g</sup> Department of Medicine, University of Padua, Italy

<sup>h</sup> Department of Surgery, Medical School, University of Cincinnati, USA

The authors regret that the references appear with the numbers in the text, while they are listed in alphabetical order in the References section. The correct reference list is the following:

### References

- [1] G.A. Gutman, K.G. Chandy, S. Grissmer, M. Lazdunski, D. McKinnon, L.A. Pardo, G.A. Robertson, B. Rudy, M.C. Sanguinetti, W. Stuhmer, X. Wang, International Union of Pharmacology. LIII. Nomenclature and molecular relationships of voltage-gated potassium channels, *Pharmacological reviews*, 57 (2005) 473–508.
- [2] A. Serrano-Albarras, I. Estadella, S. Cirera-Rocosa, M. Navarro-Perez, A. Felipe, Kv1.3: a multifunctional channel with many pathological implications, *Expert opinion on therapeutic targets*, 22 (2018) 101–105.
- [3] S. Feske, H. Wulff, E.Y. Skolnik, Ion channels in innate and adaptive immunity, *Annual review of immunology*, 33 (2015) 291–353.
- [4] G. Panyi, C. Beeton, A. Felipe, Ion channels and anti-cancer immunity, *Philosophical transactions of the Royal Society of London. Series B, Biological sciences*, 369 (2014) 20130106.
- [5] M.D. Cahalan, K.G. Chandy, The functional network of ion

channels in T lymphocytes, *Immunol Rev*, 231 (2009) 59–87.

[6] C. Beeton, H. Wulff, N.E. Standifer, P. Azam, K.M. Mullen, M.W. Pennington, A. Kolski-Andreaco, E. Wei, A. Grino, D.R. Counts, P.H. Wang, C.J. LeeHealey, S.A. B. A. Sankaranarayanan, D. Homerick, W.W. Roeck, J. Tehranzadeh, K.L. Stanhope, P. Zimin, P.J. Havel, S. Griffey, H. G. Knaus, G.T. Nepom, G.A. Gutman, P.A. Calabresi, K.G. Chandy, Kv1.3 channels are a therapeutic target for T cell-mediated autoimmune diseases, *Proceedings of the National Academy of Sciences of the United States of America*, 103 (2006) 17414–17419.

[7] S.H. Jang, S.Y. Choi, P.D. Ryu, S.Y. Lee, Anti-proliferative effect of Kv1.3 blockers in A549 human lung adenocarcinoma in vitro and in vivo, *Eur J Pharmacol*, 651 (2011) 26–32.

[8] V. Checchetto, E. Teardo, L. Carraretto, L. Leanza, I. Szabo, Physiology of intracellular potassium channels: A unifying role as mediators of counterion fluxes?, *Biochimica et biophysica acta*, 1857 (2016). 1258–1266.

[9] L. Leanza, B. Henry, N. Sassi, M. Zoratti, K.G. Chandy, E. Gulbins, I. Szabo, Inhibitors of mitochondrial Kv1.3 channels induce Bax/Bak-independent death of cancer cells, *EMBO molecular medicine*, 4

DOI of original article: <https://doi.org/10.1016/j.redox.2020.101705>.

\* Corresponding author. University of Padova, Italy.

E-mail address: [ildiko.szabo@unipd.it](mailto:ildiko.szabo@unipd.it) (I. Szabò).

<sup>1</sup> Current address: Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden.

<sup>2</sup> Current address: Biointerfaces, Swiss Federal Laboratories for Materials Science and Technology (Empa), Lerchenfeldstrasse 5, CH-9014, St. Gallen, Switzerland.

<https://doi.org/10.1016/j.redox.2021.102036>

Available online 29 June 2021

2213-2317/© 2021 Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

(2012) 577-593.

[10] L. Leanza, M. Romio, K.A. Becker, M. Azzolini, L. Trentin, A. Manago, E. Venturini, A. Zaccagnino, A. Mattarei, L. Carraretto, A. Urbani, S. Kadow, L. Biasutto, V. Martini, F. Severin, R. Peruzzo, V. Trimarco, J.H. Egberts, C. Hauser, A. Visentin, G. Semenzato, H. Kalthoff, M. Zoratti, E. Gulbins, C. Paradisi, I. Szabo, Direct Pharmacological Targeting of a Mitochondrial Ion Channel Selectively Kills Tumor Cells In Vivo, *Cancer cell*, 31 (2017) 516-531.e510.

[11] I. Szabo, J. Bock, H. Grassme, M. Soddemann, B. Wilker, F. Lang, M. Zoratti, E. Gulbins, Mitochondrial potassium channel Kv1.3 mediates Bax-induced apoptosis in lymphocytes, *Proceedings of the National Academy of Sciences of the United States of America*, 105 (2008) 14861-14866.

[12] T.P. Szatrowski, C.F. Nathan, Production of large amounts of hydrogen peroxide by human tumor cells, *Cancer research*, 51 (1991) 794-798.

[13] J. Noh, B. Kwon, E. Han, M. Park, W. Yang, W. Cho, W. Yoo, G. Khang, D. Lee, Amplification of oxidative stress by a dual stimuli-responsive hybrid drug enhances cancer cell death, *Nature communications*, 6 (2015) 6907.

[14] C. Gorrini, I.S. Harris, T.W. Mak, Modulation of oxidative stress as an anticancer strategy, *Nature reviews. Drug discovery*, 12 (2013) 931-947.

[15] E. Beraud, K.G. Chandy, Therapeutic potential of peptide toxins that target ion channels, *Inflamm Allergy Drug Targets*, 10 (2011) 322-342.

[16] A. Bartok, A. Toth, S. Somodi, T.G. Szanto, P. Hajdu, G. Panyi, Z. Varga, Margatoxin is a non-selective inhibitor of human Kv1.3 K<sup>+</sup> channels, *Toxicol: official journal of the International Society on Toxicology*, 87 (2014) 6-16.

[17] H. Wulff, P. Christophersen, P. Colussi, K.G. Chandy, V. Yarov-Yarovoy, Antibodies and venom peptides: new modalities for ion channels, *Nature reviews. Drug discovery*, 18 (2019) 339-357.

[18] A. Schmitz, A. Sankaranarayanan, P. Azam, K. Schmidt-Lassen, D. Homerick, W. Hansel, H. Wulff, Design of PAP-1, a selective small molecule Kv1.3 blocker, for the suppression of effector memory T cells in autoimmune diseases, *Molecular pharmacology*, 68 (2005) 1254-1270.

[19] P. Azam, A. Sankaranarayanan, D. Homerick, S. Griffey, H. Wulff, Targeting effector memory T cells with the small molecule Kv1.3 blocker PAP-1 suppresses allergic contact dermatitis, *The Journal of investigative dermatology*, 127 (2007) 1419-1429.

[20] P.I. Zimin, B. Garic, S.B. Bodendiek, C. Mahieux, H. Wulff, B.S. Zhorov, Potassium channel block by a tripartite complex of two cationophilic ligands and a potassium ion, *Molecular pharmacology*, 78 (2010) 588-599.

[21] S.B. Long, E.B. Campbell, R. Mackinnon, Crystal structure of a mammalian voltage-dependent Shaker family K<sup>+</sup> channel, *Science (New York, N.Y.)*, 309 (2005) 897-903.

[22] B. Hao, Z.W. Chen, X.J. Zhou, P.I. Zimin, G.P. Miljanich, H. Wulff, Y.X. Wang, Identification of phase-I metabolites and chronic toxicity study of the Kv1.3 blocker PAP-1 (5-(4-phenoxybutoxy)psoralen) in the rat, *Xenobiotica; the fate of foreign compounds in biological systems*, 41 (2011) 198-211.

[23] C. Jorgensen, L. Darre, K. Vanommeslaeghe, K. Omoto, D. Pryde, C. Domene, In silico identification of PAP-1 binding sites in the Kv1.2 potassium channel, *Molecular pharmaceuticals*, 12 (2015) 1299-1307.

[24] A. Mattarei, M. Azzolini, M. Zoratti, L. Biasutto, C. Paradisi, N-Monosubstituted Methoxy-oligo(ethylene glycol) Carbamate Ester Prodrugs of Resveratrol, *Molecules (Basel, Switzerland)*, 20 (2015) 16085-16102.

[25] S. Kundu-Raychaudhuri, Y.J. Chen, H. Wulff, S.P. Raychaudhuri, Kv1.3 in psoriatic disease: PAP-1, a small molecule inhibitor of Kv1.3 is effective in the SCID mouse psoriasis-xenograft model, *Journal of autoimmunity*, 55 (2014) 63-72.

[26] I. Szabo, L. Trentin, V. Trimarco, G. Semenzato, L. Leanza,

Biophysical Characterization and Expression Analysis of Kv1.3 Potassium Channel in Primary Human Leukemic B Cells, *Cellular physiology and biochemistry: international journal of experimental cellular physiology, biochemistry, and pharmacology*, 37 (2015) 965-978.

[27] J.A. Burger, J.G. Gribben, The microenvironment in chronic lymphocytic leukemia (CLL) and other B cell malignancies: insight into disease biology and new targeted therapies, *Seminars in cancer biology*, 24 (2014) 71-81.

[28] G.A. Smith, H.W. Tsui, E.W. Newell, X. Jiang, X.P. Zhu, F.W. Tsui, L.C. Schlichter, Functional up-regulation of HERG K<sup>+</sup> channels in neoplastic hematopoietic cells, *The Journal of biological chemistry*, 277 (2002) 18528-18534.

[29] L. Leanza, L. Trentin, K.A. Becker, F. Frezzato, M. Zoratti, G. Semenzato, E. Gulbins, I. Szabo, Clofazimine, Psora-4 and PAP-1, inhibitors of the potassium channel Kv1.3, as a new and selective therapeutic strategy in chronic lymphocytic leukemia, *Leukemia*, 27 (2013) 1782-1785.

[30] R. Costa, R. Peruzzo, M. Bachmann, G.D. Monta, M. Vicario, G. Santinon, A. Mattarei, E. Moro, R. Quintana-Cabrera, L. Scorrano, M. Zeviani, F. Vallese, M. Zoratti, C. Paradisi, F. Argenton, M. Brini, T. Cali, S. Dupont, I. Szabo, L. Leanza, Impaired Mitochondrial ATP Production Downregulates Wnt Signaling via ER Stress Induction, *Cell reports*, 28 (2019) 1949-1960.e1946.

[31] S.B. Bodendiek, C. Mahieux, W. Hansel, H. Wulff, 4-Phenoxybutoxy-substituted heterocycles—a structure-activity relationship study of blockers of the lymphocyte potassium channel Kv1.3, *Eur J Med Chem*, 44 (2009) 1838-1852.

[32] S.R. Chiang, C.S. Lin, H.H. Lin, P.C. Shieh, S.H. Kao, Bergapten induces G1 arrest of nonsmall cell lung cancer cells, associated with the p53mediated cascade, *Molecular medicine reports*, 19 (2019) 1972-1978.

[33] M.C. Cholo, H.C. Steel, P.B. Fourie, W.A. Germishuizen, R. Anderson, Clofazimine: current status and future prospects, *J Anti-microb Chemother*, 67 (2012) 290-298.

[34] S. Marzian, P.J. Stansfeld, M. Rapedius, S. Rinne, E. Nematian-Ardestani, J.L. Abbruzzese, K. Steinmeyer, M.S. Sansom, M.C. Sanguinetti, T. Baukowitz, N. Decher, Side pockets provide the basis for a new mechanism of Kv channel-specific inhibition, *Nat Chem Biol*, 9 (2013) 507-513.

[35] A. Cabrera-Orefice, E.G. Yoga, C. Wirth, K. Siegmund, K. Zwicker, S. Guerrero-Castillo, V. Zickermann, C. Hunte, U. Brandt, Locking loop movement in the ubiquinone pocket of complex I disengages the proton pumps, *Nature communications*, 9 (2018) 4500.

[36] C. Wirth, U. Brandt, C. Hunte, V. Zickermann, Structure and function of mitochondrial complex I, *Biochimica et biophysica acta*, 1857 (2016) 902-914.

[37] E.M. Pasciak, J.T. Rittichier, C.H. Chen, M.S. Mubarak, M.S. VanNieuwenhze, D.G. Peters, Electroreductive dimerization of coumarin and coumarin analogues at carbon cathodes, *The Journal of organic chemistry*, 80 (2015) 274-280.

[38] J. Trnka, M. Elkalaf, M. Anděl, Lipophilic triphenylphosphonium cations inhibit mitochondrial electron transport chain and induce mitochondrial proton leak, *PLoS one*, 10 (2015) e0121837.

[39] P. Bednarczyk, M.R. Wieckowski, M. Broszkiewicz, K. Skowronek, D. Siemen, A. Szewczyk, Putative Structural and Functional Coupling of the Mitochondrial BK Channel to the Respiratory Chain, *PLoS one*, 8 (2013) e68125.

[40] A.P. Wojtovich, C.O. Smith, C.M. Haynes, K.W. Nehrke, P.S. Brookes, Physiological consequences of complex II inhibition for aging, disease, and the mKATP channel, *Biochimica et biophysica acta*, 1827 (2013) 598-611.

[41] A. Paggio, V. Checchetto, A. Campo, R. Menabo, G. Di Marco, F. Di Lisa, I. Szabo, R. Rizzuto, D. De Stefani, Identification of an ATP-sensitive potassium channel in mitochondria, *Nature*, 572 (2019) 609-613.

[42] L. Carraretto, E. Teardo, V. Checchetto, G. Finazzi, N. Uozumi, I.

Szabo, Ion Channels in Plant Bioenergetic Organelles, Chloroplasts and Mitochondria: From Molecular Identification to Function, *Molecular plant*, 9 (2016) 371-395.

[43] L. Leanza, M. Zoratti, E. Gulbins, I. Szabo, Induction of apoptosis in macrophages via Kv1.3 and Kv1.5 potassium channels, *Current medicinal chemistry*, 19 (2012) 5394-5404.

[44] N. Comes, J. Bielanska, A. Vallejo-Gracia, A. Serrano-Albarras, L. Marruecos, D. Gomez, C. Soler, E. Condom, Y.C.S. Ramon, J. Hernandez-Losa, J.C. Ferreres, A. Felipe, The voltage-dependent K(+) channels Kv1.3 and Kv1.5 in human cancer, *Frontiers in physiology*, 4 (2013) 283.

[45] M. Zoratti, I. Szabo, The mitochondrial permeability transition, *Biochimica et biophysica acta*, 1241 (1995) 139-176.

[46] I. Szabo, B. Nilius, X. Zhang, A.E. Busch, E. Gulbins, H. Suessbrich, F. Lang, Inhibitory effects of oxidants on n-type K<sup>+</sup> channels in T lymphocytes and *Xenopus oocytes*, *Pflugers Archiv: European journal of physiology*, 433 (1997) 626-632.

[47] F. Duprat, E. Guillemare, G. Romey, M. Fink, F. Lesage, M. Lazdunski, E. Honore, Susceptibility of cloned K<sup>+</sup> channels to reactive oxygen species, *Proceedings of the National Academy of Sciences of the United States of America*, 92 (1995) 11796-11800.

[48] J.L. Bowling, M.C. Skolfield, W.A. Riley, A.P. Nolin, L.C. Wolf,

D.E. Nelson, Temporal integration of mitochondrial stress signals by the PINK1:Parkin pathway, *BMC molecular and cell biology*, 20 (2019) 33.

[49] Y. Yao, M. Xue, J. Chen, M. Zhang, F. Huang, An amphiphilic pillar[5]arene: synthesis, controllable self-assembly in water, and application in calcein release and TNT adsorption, *J Am Chem Soc*, 134 (2012) 15712-15715.

[50] F. Frezzato, V. Trimarco, V. Martini, C. Gattazzo, E. Ave, A. Visentin, A. Cabrelle, V. Olivieri, R. Zambello, M. Facco, F. Zonta, A. Cristiani, A.M. Brunati, S. Moro, G. Semenzato, L. Trentin, Leukemic cells from chronic lymphocytic leukemia patients undergo apoptosis following microtubule depolymerization and Lyn inhibition by noco-dazole, *British journal of haematology*, 165 (2014) 659-672.

[51] C. Frezza, S. Cipolat, L. Scorrano, Organelle isolation: functional mitochondria from mouse liver, muscle and cultured fibroblasts, *Nature protocols*, 2 (2007) 287-295.

[52] C. Glytsou, E. Calvo, S. Cogliati, A. Mehrotra, I. Anastasia, G. Rigoni, A. Raimondi, N. Shintani, M. Loureiro, J. Vazquez, L. Pellegrini, J.A. Enriquez, L. Scorrano, M.E. Soriano, Optic Atrophy 1 Is Epistatic to the Core MICOS Component MIC60 in Mitochondrial Cristae Shape Control, *Cell reports*, 17 (2016) 3024-3034.

The authors would like to apologise for any inconvenience caused.