Professional profile of György Panyi

Current affiliation

György Panyi, M.D., Ph.D., D.Sc.
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Personal details

Born (date, place): 1966. September 20. Vásárosnamény, Hungary
Marital status: dr. Ildikó Gődény (1991), Children: Zsófia ('93), Dávid ('96)

Education and degrees

1991: University Medical School of Debrecen, Faculty of Medicine, Medical Doctor
1996: Ph.D., University Medical School of Debrecen, Hungary
2005: D.Sc., Hungarian academy of Sciences

Past appointments

1991-1992: Research fellow, Hungarian Academy of Sciences
1992-1997: Research assistant, U. Med. School of Debrecen, Dept. of Biophysics
1994-1996: Visiting scholar, University of Pennsylvania, Dept. of Physiology, USA
1997-2002: Assistant professor, U. Med. School of Debrecen, Dept. of Biophysics

Fellowships

1994-1996: Fogarty International Research Fellowship, NIH, USA
1998-2001: János Bolyai Research Scholarship, Hungarian Academy of Sciences
2002-2003: György Békési Fellowship, Hungarian Ministry of Education
2005-2008: János Bolyai Research Scholarship, Hungarian Academy of Sciences
2005-2006: National Institute of Neurological Disorders and Stroke fellowship, NIH, USA

Graduated Ph.D. students

2001: Mózes Péter
2003: Péter Hajdú
2005: Miklós Bagdány

Membership in professional societies, editorial and reviewer duties

1991: Society of Hungarian Immunologists
1992: Hungarian Biophysical Society, secretary of the Ion Channel committee (2004)
1994: Biophysical Society (USA)
Ad hoc reviewer for the European Journal of Biophysics, Journal of Physiology (London), Journal of Photochemistry and Photobiology B: Biology

Awards

1991: Pro Scientia Gold Medal (Hungarian Ministry of Education)
1991: István Weszprémi prize (University Medical School of Debrecen)
1997: Young investigator award, Hungarian Biophysical Society
2001: Pro Scientia Gold Medal, tutor (Hungarian Ministry of Education)

2002, 2004: Lecturer of the Year (from Univ. of Debrecen, Faculty of Medicine)
2005: EBSA Prize

Scientific interest, major achievements and collaborators
Research projects in the laboratory focus on two types of ion channels of T-lymphocytes, the voltage-gated K+ channel, Kv1.3, and the Ca2+-activated K+ channel, IKCa1. These channels are important for the regulation of membrane potential dependent processes in T cells, such as mitogen-stimulated proliferation. Understanding the biophysical properties of Kv1.3 and its regulation may be critical to our comprehension of T-cell physiology and immune responsiveness. Past and ongoing research projects in the laboratory fall into three major categories:

1. Molecular pharmacology of T-cell ion channels. Our main focus is on peptide toxins isolated from scorpion venoms and the aim is to identify toxins that block these channels with high affinity and selectivity. Since block of Kv1.3 channels inhibits proliferation, these blockers could serve as templates for the development of high affinity and high specificity drugs for the treatment of diseases affecting the immune system. In the past we have identified one of the highest affinity Kv1.3 inhibitors, Pi2, from the scorpion Pandinus imperator (Kd: 44 pM) (J Membr Biol 2001;179:13-25.). We also identified the first Kv1.3 blocker (Tc32) lacking the essential diad of critically positioned amino acids previously claimed to be required for K+ channel recognition (Biochim Biophys Acta 2002;1601:123-131.). Anuroctoxin, a peptide blocker of Kv1.3 channels described recently in our laboratory, is highly selective for Kv1.3 channels over other Shaker-related voltage-gated potassium channels and the Ca2+-activated K+ channels of T lymphocytes (Mol Pharmacol. 2005; 67:1034-44.). Due to its high selectivity and affinity for Kv1.3, Anuroctoxin is currently tested for its in vivo immunosuppressive effect.
Major collaborator: Prof. Lourival Possani, National Autonomous University of Mexico, Mexico, Dept. of Molecular Recognition and Structural Biology

2. Distribution of Kv1.3 channels in the lymphocyte membrane. The lateral distribution of Kv1.3 channels in the T-cell membrane was studied to reveal intermolecular interactions between the channel and the surrounding membrane lipids and functionally important proteins. In these experiments we combined electrophysiology with advanced fluorescence microscopy and flow cytometry. We found that Kv1.3 channels are non-randomly distributed in the plasma membrane and their distribution shows significant overlap with that of T cell receptor/CD3 molecules; the two molecules are in molecular proximity (Proc Natl Acad Sci U S A 2003;100:2592-2597). Kv1.3 channels are redistributed in the membrane of cytotoxic lymphocytes when they come into contact with a target cell and an immunological synapse is formed between them (Proc Natl Acad Sci U S A 2004;101:1285-1290). We also described the lipid raft association of Kv1.3 channels and the significant effect of the modification of the cholesterol content of the plasma membrane of T cells on the activation and inactivation kinetics of Kv1.3 channels (Pflugers Arch 2003;445:674-682). The relocation of Kv1.3 channels into different membrane domains and in the proximity of signaling molecules gathered at the immunological synapse probably plays a role in the fine tuning of the signal transduction pathway of T cells (Trends Immunol 2004. 25:565-569).

3. Biophysics of Kv1.3 channels: Inactivation of voltage-gated potassium channels limits the K+ conductance available for the membrane-potential control of the cells. Analyzing the inactivation kinetics of homo- and heterotetrameric channels

composed of mutant and wild-type subunits we showed that the four subunits of a given channel interact cooperatively to determine the inactivation rate (Biophys J 1995;69:896-904). Based on this framework of experimental approach and mathematical analysis we described that subunits of teterameric channels assembled during the biogenesis do not dissociate and re-associate in the plasma membrane (J Gen Physiol 1996;107:409-420). Using biophysical and molecular biological methods our laboratory identified the molecular mechanism being responsible for the effects of the extracellular acidification on the inactivation kinetics of Kv1.3 channels. We showed that protonation of His399 in the channel pore creates an energy barrier for K+ ions to leave the pore thereby slowing inactivation (Am J Physiol Cell Physiol 2004;287:C1067-C1076).
Major collaborator: Prof. Carol Deutsch, University of Pennsylvania, USA, Dept. of Physiology.

List of Publications

Papers in peer reviewed journals

1. Bagdany, M., Batista, C.V., Valdez-Cruz, N.A., Somodi, S., Rodriguez de la Vega RC, Licea, A.F., Varga, Z., Gaspar, R., Possani, L.D., and Panyi, G.: Anuroctoxin, a new scorpion toxin of the alpha-KTx 6 subfamily, is highly selective for Kv1.3 over IKCa1 ion channels of human T lymphocytes. Mol. Pharmacol. 67, 1034-1044, 2005.
2. Detre, C., Kiss, E., Varga, Z., Ludanyi, K., Paszty, K., Enyedi, A., Kovesdi, D., Panyi, G., Rajnavolgyi, E., and Matko, J.: Death or survival: Membrane ceramide controls the fate and activation of antigen-specific T-cells depending on signal strength and duration. Cell Signal., (in press) 2005.
3. Olamendi-Portugal, T., Somodi, S., Fernandez, J.A., Zamudio, F.Z., Becerril, B., Varga, Z., Panyi, G., Gaspar, R., and Possani, L.D.: Novel alpha-KTx peptides from the venom of the scorpion Centruroides elegans selectively blockade Kv1.3 over IKCa1 K+ channels of T cells. Toxicon 46, 418-429, 2005.
4. Batta, T.J., Panyi, G., Szucs, A., and Sziklai, I.: Regulation of the lateral wall stiffness by acetylcholine and GABA in the outer hair cells of the guinea pig. Eur. J Neurosci. 20, 3364-3370, 2004.
5. Hajas, G., Zsiros, E., Laszlo, T., Hajdu, P., Somodi, S., Rethi, B., Gogolak, P., Ludanyi, K., Panyi, G., and Rajnavolgyi, E.: New phenotypic, functional and electrophysiological characteristics of KG-1 cells. Immunol. Lett. 92, 97-106, 2004.
6. Panyi, G., Vamosi, G., Bacso, Z., Bagdany, M., Bodnar, A., Varga, Z., Gaspar, R., Matyus, L., and Damjanovich, S.: Kv1.3 potassium channels are localized in the immunological synapse formed between cytotoxic and target cells. Proc. Natl. Acad. Sci. U. S. A 101, 1285-1290, 2004.
7. Somodi, S., Varga, Z., Hajdu, P., Starkus, J.G., Levy, D.I., Gaspar, R., and Panyi, G.: pH dependent modulation of Kv1.3 inactivation: the role of His399. Am. J Physiol Cell Physiol 287, C1067-C1076, 2004.
8. Szucs, A., Szappanos, H., Toth, A., Farkas, Z., Panyi, G., Csernoch, L., and Sziklai, I.: Differential expression of purinergic receptor subtypes in the outer hair cells of the guinea pig. Hear. Res 196, 2-7, 2004.
9. Batta, T.J., Panyi, G., Gaspar, R., and Sziklai, I.: Active and passive behaviour in the regulation of stiffness of the lateral wall in outer hair cells of the guinea-pig. Pflugers Arch. 447, 328-336, 2003.
10. Hajdu, P., Varga, Z., Pieri, C., Panyi, G., and Gaspar, R., Jr.: Cholesterol modifies the gating of Kv1.3 in human T lymphocytes. Pflugers Arch. 445, 674-682, 2003.
11. Hajdu, P., Ulens, C., Panyi, G., and Tytgat, J.: Drug- and mutagenesis-induced changes in the selectivity filter of a cardiac two-pore background K+ channel. Cardiovasc. Res. 58, 46-54, 2003.
12. Panyi, G., Bagdany, M., Bodnar, A., Vamosi, G., Szentesi, G., Jenei, A., Matyus, L., Varga, S., Waldmann, T.A., Gaspar, R., and Damjanovich, S.: Colocalization and

nonrandom distribution of Kv1.3 potassium channels and CD3 molecules in the plasma membrane of human T lymphocytes. Proc. Natl. Acad. Sci. U. S. A. 100, 2592-2597, 2003.
13. Batista, C.V., Gomez-Lagunas, F., Rodríguez de la Vega RC, Hajdu, P., Panyi, G., Gaspar, R., and Possani, L.D.: Two novel toxins from the Amazonian scorpion Tityus cambridgei that block Kv1.3 and Shaker B K(+)-channels with distinctly different affinities. Biochim. Biophys. Acta 1601, 123-131, 2002.
14. Nagy, P., Matyus, L., Jenei, A., Panyi, G., Varga, S., Matkó, J., Szollosi, J., Gaspar, R.Jr., Jovin, T.M., and Damjanovich, S.: Cell Fusion Experiments Reveal Distinctly Different Association Characteristics of Cell Surface Receptors. J. Cell Sci. 114, 4063-4071, 2001.
15. Peter, M.J., Varga, Z., Hajdu, P., Gaspar, R.J., Damjanovich, S., Horjales, E., Possani, L.D., and Panyi, G.: Effects of toxins Pi2 and Pi3 on human T lymphocyte Kv1.3 channels: the role of Glu7 and Lys24. J Membr. Biol 179, 13-25, 2001.
16. Varga, Z., Panyi, G., Péter, M., Pieri, C., Csécsei, G., Damjanovich, S., and Gáspár, R.: Multiple binding sites for melatonin on Kv1.3. Biophys. J. 80, 1280-1297, 2001.
17. Peter, M., Hajdu, P., Varga, Z., Damjanovich, S., Possani, L.D., Panyi, G., and Gaspar, R.: Blockage of human T lymphocyte Kv1.3 channels by Pi1, a novel class of scorpion toxin. Biochem. Biophys. Res. Commun. 278, 34-37, 2000.
18. Peter, M., Varga, Z., Panyi, G., Bene, L., Damjanovich, S., Pieri, C., Possani, L.D., and Gaspar, R.: Pandinus imperator scorpion venom blocks voltage-gated K+ channels in human lymphocytes. Biochem. Biophys. Res. Commun. 242, 621-625, 1998.
19. Panyi, G., Gáspár, R., Krasznai, Z., ter Horst, J.J., Ameloot, M., Aszalós, A., Steels, P., and Damjanovich, S.: Immunosuppressors inhibit voltage-gated potassium channels in human peripheral blood lymphocytes. Biochem. Biophys. Res. Commun. 221, 254-258, 1996.
20. Panyi, G. and Deutsch, C.: Assemby and suppression of endogenous Kv1.3 channels in human T cells. J. Gen. Physiol. 107, 409-420, 1996.
21. Nagy, P., Panyi, G., Jenei, A., Bene, L., Gáspár, R., Matkó, J., and Damjanovich, S.: Ion channel activities regulate transmembrane signaling in thymocyte apoptosis and T-cell activation. Immunol. Lett. 44, 91-95, 1995.
22. Panyi, G., Sheng, Z.-F., Tu, L.-W., and Deutsch, C.: C-type inactivation of a voltage-gated K+ channel occurs by a cooperative mechanism. Biophys. J. 69, 896-904, 1995.
23. Vereb, G., Matyus, L., Bene, L., Panyi, G., Bacso, Z., Balazs, M., Matkó, J., Szollosi, J., Gaspar, R.Jr., and Damjanovich, S.: Plasmamembranebound macromolecules are dynamically aggregated to form nonrandom codistribution patterns of selected functional elements. Do pattern recognition processes govern antigen presentation and intercellular interactions? J. Mol. Recognit. 8, 237-246, 1995.
24. Gáspár, R., Panyi, G., Krasznai, Z., Ypey, D.L., Vereb, Gy., Pieri, C., and Damjanovich, S.: Effects of Bretylium Tosilate on Voltage-Gated Potassium Channels in Human T Lymphocytes. Mol. Pharmacol. 46, 762-766, 1994.
25. Panyi, G., Berecki, G., Gáspár, R., Seres, I., Fülöp, T., and Damjanovich, S.: Peripheral blood lymphocytes display reduced K+ channel activity in aged humans. Biochem. Biophys. Res. Commun. 199, 519-524, 1994.
26. Matkó, J., Nagy, P., Panyi, G., Vereb, G., Bene, L., Mátyus, L., and Damjanovich, S.: Biphasic effect of extracellular ATP on the membrane potential of mouse thymocytes. Biochem. Biophys. Res. Commun. 191, 378-384, 1993.
27. Weidema, A.F., Ravesloot, J.H., Panyi, G., Nijweide, P., and Ypey, D.L.: A Ca2+-dependent K+-channel in freshly isolated and cultured chick osteoclasts. Biochim. Biophys. Acta 1149, 63-72, 1993.
28. Vereb, G., Panyi, G., Balázs, M., Mátyus, L., Matkó, J., and Damjanovich, S.: Effect of cyclosporin A on the membrane potential and Ca2+ level of human lymphoid cell lines and mouse thymocytes. Biochim. Biophys. Acta 1019, 159-165, 1990.

Review papers

1. Panyi, G.: Biophysical and pharmacological aspects of K+ channels in T lymphocytes. Eur. Biophys. J. 34, 515-529, 2005.
2. Damjanovich, S., Gaspar, R.J., and Panyi, G.: An alternative to conventional immunosuppression: small-molecule inhibitors of Kv1.3 channels. Mol Intervent 4, 251-254, 2004.
3. Panyi, G., Varga, Z., and Gaspar, R.: Ion channels and lymphocyte activation. Immunol. Lett. 92, 55-66, 2004.
4. Panyi, G., Vamosi, G., Bodnar, A., Gaspar, R.J., and Damjanovich, S.: Looking through ion channels: recharged concepts in T cell signaling. Trends Immunol. 25, 565-569, 2004.

Book chapters

1. Gaspar, R., Varga, Z., Panyi, G., Krasznai, Z., Pieri, C., and Damjanovich, S.: Measurement and analysis of different aspects of potassium currents in human lymphocytes. In: Signal transduction-Single cell techniques. Springer Lab Manual, edited by Van Duijn, B., and Wiltink, A., Berlin, Heidelberg, New York: Springer-Verlag, 1998; 214-235.
2. Krasznai, Z., Weidema, A.F., Gaspar, R., Panyi, G., and Ypey, D.L.: Ionic conductances in chicken osteoclasts. In: Signal Transduction-Single cell techniques. Springer Lab Manual, edited by Van Duijn B and Wiltink A. Berlin, Heidelberg, New York: Springer-Verlag, 1998; 236-245.
3. Panyi, G.: Heterologous expression of ion channel genes: combination of molecular biology and electrophysiology. In: Practical guide to physical analysis of cell surface receptors, edited by Krasznai Z and Mátyus L. Debrecen: Department of Biophysics and Cell Biology, University Medical School of Debrecen, 1998; 17-40.
4. Peter, M., Varga, Z., Krasznai, Z., Panyi, G., and Gaspar, R.: Recording and analysis of membrane potential and ion currents in cultured peripheral human lymphocytes. In: Practical guide to physical analysis of cell surface receptors, edited by Krasznai Z and Mátyus L. Debrecen: Department of Biophysics and Cell Biology, University Medical School of Debrecen, 1998; 1-16.
5. Panyi, G., Somodi, S., Varga, Z., Hajdu, P., Pandi-Perumal, S.R., Damjanovich, S., and Gaspar, R.: Pharmacological effects of melatonin on ion channels. In: Treatise on pineal gland and melatotin, edited by Haldar C, Singaravel M and Maitra KS. Enfield, USA; Plymouth, UK: Science Publishers Inc., 2003; 491-508.