CURRICULUM VITAE

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Matthias A. Hediger

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1. Personal Data				
	August 7, 1953	Nationality:	Swiss	Y
Civil status:	Married, one child	ORCID	<u>0000-0003-1946-027X</u>	
2. Education and training				
1983	Dr. sc. nat. ETH (Ph.D.)	Swiss Federal	I Institute of Technology,	Switzerland
1977	Dipl. sc. nat. (Biochemistry)	Swiss Federal	I Institute of Technology,	Switzerland
3. Employment				
Professional Positions:				
2019-	Head of Membrane Transport Discovery Lab & Senior Researcher, Department of Nerology and Hypertension, University Hospital Bern Inselspital, Bern, Switzerland.			
2019-	Professor em., Institute of Biochemistry and Molecular Medicine, University of Bern, Switzerland.			
2005-2019	Professor Ordinarius, Institute of Biochemistry and Molecular Medicine,			
	University of Bern, Switzerland.			
1995-2005	Associate Professor of Medicine (Biological Chemistry and Molecular Pharmacology),			
	Harvard Medical School, Boston, MA, USA.			
1989-1995	Assistant Professor of Medicine, Harvard Medical School, Boston, MA, USA.			
1986-1989	Assistant Research Physiologist, Dept. of Physiology, UCLA School of Medicine, Los			
	Angeles, CA, USA.			
1984-1986	6 Postgraduate Research Biochemist, Dept. of Biological Chemistry, UCLA School of			
Medicine, Los Angeles, CA, USA.				
1982-1983	Postgraduate Research Biochemist, Dept. of Biochemistry, University of			
	Connecticut Health Center, H	· •	•	•
4. Institutional responsibilities:				
2005-2017 Director, Institute of Biochemistry and Molecular Medicine, University of Bern, Switzer				
	land.	2		.
2010-2014	Director, NCCR TransCure	the Swiss Nati	onal Center of Competen	ce in Research.
	TransCure), Medical Faculty		1	,
1999-2005	Director, Membrane Biology Program, Brigham and Women's Hospital,			
	Harvard Medical School, Bo		1	,
5. Research grants (PI: Hediger MA)				

- 1. *The role of neutral amino acid transporters in colorectal cancer progression.* Swiss Cancer League, PI Matthias Hediger. Co-PI Inti Zlobec. May 1, 2017 April 30, 2020.
- 2. Compound screening on solute carrier SLC15A4 to targeting for lupus autoimmune disease. CTI, PI Matthias Hediger. Funding period: June 1, 2018 – November 30, 2019 (with "cost-neutral" extension till March 31, 2020).
- 3. *The role of mitochondrial carriers in metabolic tuning and reprogramming by calcium flow across membrane contact sites.* Sinergia, Swiss National Science Foundation. PI Matthias Hediger, Co-PI Martin Lochner and Edmund Kunji. Funding period: September 1, 2018 August 31, 2022.

- 4. *Intestinal absorption of transition metals in human health and disease*. Swiss National Science Foundation. PI Matthias Hediger, February 1, 2019 January 31, 2023.
- 5. Optogenetic control of the ER calcium store release by a novel ER-localized photoactivated cation channel. Spark «Rapid funding of unconventional ideas», Swiss National Science Foundation. PI Matthias Hediger, December 1, 2019 – November 30, 2020.

Submitted:

6. *Molecular mechanisms of TRPV channel function: Towards novel therapeutic approaches.* Swiss National Science Foundation. PI Matthias Hediger

6. Supervision of junior researchers at graduate and postgraduate level

- 1. Supervision and training of bachelor and master students (past 10 years): Current Master student are Jan Dernič. Recent master theses were completed by Marina Troxler, Mey Boukenna, Damian Nydegger, Stefanie Graeter, Andrea Amati, etc.
- 2. Doctoral theses in biology (past 10 years): Current PhD student is Damian Nydegger (ongoing). Recent master theses were completed by Mey Boukenna (2019), Marie-Christine Franz (2015), Marc Bürzle (2012), Katrin A. Bolanz (January 2010).
- 3. Over the past 25 years, Matthias Hediger has supervised and trained 44 post-doctoral researchers.

7. Teaching activities

Membrane Biochemistry (yearly Master lecture series (ongoing), lectures to veterinary medicine (VetSuisse) and medical students (until 2018); head of Endocrinology Block for 2nd year medical students (until 2018).

8. Memberships in panels, boards, etc., and individual scientific reviewing activities

- 2005-2019 Participation at regular faculty meetings of the Medical Faculty, University of Bern. Delegate of numerous faculty recruitment and habilitation evaluation committees on behalf of the University of Bern
- 2003-2005 Vice Chair, Steering Committee, Epithelial Transport Group, Am. Physiol. Society
- 1995- Specialist Advisor, HUGO Gene Nomenclature Committee (<u>http://www.genenames.org</u>)
- 1995 Partners Research Task Force of Massachusetts General Hospital and Brigham and Women's Hospital, Harvard Medical School to support new joint studies
- 1989- Ongoing peer review (Science, Nature, Cell, PNAS, Nature Commun, eLife, etc.)

9. Active memberships in scientific societies, fellowships in renowned academies

Ongoing American Physiological Society (APS), International BioIron Society (IBS), Life Sciences Switzerland (LS2), Biochemische Vereinigung Bern (BVB)

10. Organization of conferences (past 10 years)

- 2019 Organizer BioMedical Transporters Conference, Lucerne, Swiss Museum of Transport "Membrane transporters and channels: From basic research to drug" August 4-8
- 2017 Organizer BioMedical Transporters Conference, Lausanne, Olympic Museum, "SLC Transporters and Ion Channels in Drug Discovery and Preclinical Development" August 6-10
- 2015 Organizer BioMedical Transporters Conference, Lugano, Palazzo dei Congressi "Membrane Transporters – from Basic Science to Drug Discovery" August 9-13
- 2013 Organizer BioMedical Transporters Conference, St. Moritz, Hotel Laudinella "Transporters and Channels in Drug Discovery and Preclinical Development", August 11-15
- 2011 Organizer BioMedical Transporters Conference, Grindelwald Congress Center "Membrane Transporters in Drug Discovery", August 7-11

2009 Organizer and Chair, USGEB Meeting 2009: Membranes in Motion, January 29-30, Interlaken, Switzerland <u>http://www.bioparadigms.org/biomedical09/USEGB%202009/index.html</u>

11. Prizes, awards, fellowships

- 2018 Special Award, MDO/JSSX International Joint Meeting, Kanazawa, Japan.
 2009 Japanese Society for the Study of Xenobiotics Award (Kyoto, Japan)
- 2003 Rank Prize Funds, Surrey, UK Award in recognition of work on the identification, molecular characterization and control of cellular nutrient transporters
- 1998 Recipient of an award to support interdisciplinary and interdepartmental research at Brigham and Women's Hospital
- 1996 Visiting Professor, University College London
- 1989 Annual Award for Excellence in Renal Research in recognition of research of the human Na⁺/glucose cotransporters. American Physiological Society
- **12.** Career breaks None

Research focus and scientific achievements – Matthias A. Hediger

Research arising from the laboratory of Matthias Hediger has historically focused on functional characterization of clinically important membrane transporters and ion channels using a variety of methodologies such as electrophysiology, transport studies, structure function analysis, advanced imaging technologies and bioinformatics. Over the past 20 years, his studies have revealed the mechanistic foundations for transporters of iron (SLC11A2), vitamin C (SVCT1 and SVCT2), urea (SLC14A2), citrate (SLC13A2), glutamate (SLC1A1), dibasic amino acids (SLC3A1), peptides (SLC15A1), as well as for the epithelial calcium channels TRPV5 and TRPV6 and the Orai calcium channels. Most recent efforts have focused on combining knowledge from atomic structures of these proteins with computational modelling, MD simulations, site-directed mutagenesis and chemistry to reveal new insights into the translocation and gating mechanisms of transporters and channels and to develop pharmaceutical modulators of medically important transport proteins.

Establishment of NCCR TransCure

The National Centre of Competence in Research (NCCR) "*TransCure*" has been initiated and directed by Matthias Hediger starting in year 2010, with the main goal to accelerate the transformation of knowledge from basic research within the transporter/channel field into use. The leading house of this network is the University of Bern (<u>https://www.nccr-transcure.ch/about-us/</u>), and it is currently ran by Hugues Abriel. Our network is composed of a dozen multidisciplinary scientific laboratories affiliated at Universities in Basel, Bern, Lausanne and Zurich. This team of Swiss academic experts are focused on cellular membrane transporter/channel research and emerging applications for the treatment of human diseases. Using TransCure's approach "*from transport physiology to the identification of therapeutic targets*" researchers are working collaboratively, combining a unique interdisciplinary skill-set that encompasses three major disciplines, referred to as "TransCure Trias": Physiology/Medicine, Structural Biology and Medicinal Chemistry. The NCCR TransCure projects are expected to accelerate the development of therapeutic strategies, ultimately to improve human health.

Current projects and recent achievements:

Calcium channel TRPV6 in health and disease: As part of the initial activities of the NCCR TransCure network, we have been working with the group of Jean-Louis Reymond to look for specific TRPV6 inhibitors. Our effort has led to the generation of the first inhibitor, cis-22a, that exhibits a remarkable specificity, with an IC50 value in the subnanomolar range (Angew Chem Int Ed Engl. 2015; 54:14748-52). Recent efforts have focused on studies of human TRPV6 mutants that show altered inhibition with cis22a compared to wt. Interestingly, certain mutants of residues of the 2APB binding pocket also exhibit reduced inhibition by cis-22a. The 2015 "Angewandte Chemie" paper also included molecular docking calculations for cis-22a that our lab performed using an in-house created model of TRPV6 based on the previously published structure of TRPV1. In collaboration with Jean-Louis Reymond and Christoph Romanin, we developed a novel photoswitchable

inhibitor of TRPV6 that is expected to serve as a versatile tool compound to deepen our understanding of TRPV6 (**ACS Med Chem Lett. 2019; 10:1341-1345**). In addition, our first paper on capsaicin derivatives and their effects on TRPV1 and TRPV6 channel function has recently been released (**Bioorg Med Chem. 2019;27:2893-2904**).

- 2. Structure, function and pharmacology of Orai/STIM calcium channels: In year 2015, our laboratory got awarded a Swiss-Sinergia interdisciplinary research grant entitled "Store-operated calcium channels in health and disease", together with Nicolas Demaurex (Cellular Physiologist, University of Geneva, Switzerland) and Martin Lochner, we therefore became engaged in numerous projects on SOCE and STIM. This work is just now beginning to yield publications, and the first couple of papers already came out, published in collaboration with Nicolas Demaurex (J Physiol. 2019 597:561-582), as well as Christoph Romanin and Jean-Louis Reymond (Cell Calcium. 2019;79: 57-67). Manuscripts on several topics related to the Orai/STIM structure, function and pharmacology are currently being written up for publication.
- 3. Structure, function and therapeutic implications of the SLC11A2/DMT1 iron transporter: After the molecular discovery of the divalent metal ion transporter by our group (Nature. 1997, 388:482-8), Raimund Dutzler, as part of the NCCR TransCure iron project, reported the 3D structure of DMT1/SLC11A2 from Staphylococcus capitis (ScaDMT), unveiling it as a LeuT-fold transporter. As a follow-up, we employed molecular dynamics simulations and site-directed mutagenesis and discovered a novel H⁺ transfer mechanism in DMT1. Our molecular dynamics simulations provided first insight into how H⁺-translocation through E193 is allosterically linked to intracellular gating, revealing a novel H⁺-coupling mechanism that is distinct from that of other H⁺-transporters (Sci Rep. 2017 ;7:6194). The mechanistic base of the inhibition of DMT1 has recently been elucidated for bis-isothiourea substituted compounds in collaboration with the groups of Raimund Dutzler (University of Zurich and Jean-Louis Reymond (University of Bern) and our paper on this topic has now just been accepted by eLife.
- 4. SLC39/ZIP metal ion transporters and in pathologies: A combination of *in silico* and *in vitro* techniques involving structural modeling, mutagenesis and functional characterization was employed to unravel the structural elements of pH sensitivity and substrate binding in the human zinc transporter SLC39A2 (ZIP2), thereby providing the first structural evidence for the previously observed pH and voltage modulation of ZIP2-mediated metal transport (J Biol Chem. 2019;294:8046-8063). An inhibitor against the SLC39A8/ZIP8 zinc transporter has recently been generated and will be tested using an in vitro osteoarthritis cellular system, looking for beneficial disease treatment effects.
- 5. Role of amino acid transporters in colorectal cancer progression: Our recent data reveal that oncogenic mutations boost amino acid delivery into colorectal cancer cells via Hippo-mediated upregulation of specific amino acid transporters (manuscript in preparation)
- 6. **Peptide/histidine transporter SLC15A4:** Investigation of the biology of the orphan endosomal peptide/histidine transporter SLC15A4 has led to the development of therapeutic hit compounds that target this transporter. These are currently being evaluated with respect to application to the treatment of autoimmune diseases such as systemic lupus erythematosus (SLE) and inflammatory bowel disease (IBD).
- 7. **Glial glutamate transporters (SLC1A2/GLT1):** Our recent collaboration with Rodan, Lance, Children's Hospital, Harvard Medical School revealed novel glutamate transporter mutations that cause epilepsy via a dominant negative mechanism. We found that these mutations are localized in the trimerization domain of the glutamate transporter trimers (**Ann Neurol. 2019;85:921-926**).

Conference organization

Matthias Hediger has established two different international conference series to promote the transporter/ion channel field in the biomedical and pharmaceutical areas:

- 1) International Gordon Research Conference Series on transporters and channels
- 2) International BioMedical Transporter Conference Series (held biennially) on the pharmaceutical aspects of transporters and channels. The focus is on transporter and ion channel-based drug discovery strategies,

pharmacokinetics, drug delivery and drug elimination (<u>http://www.bioparadigms.org/confer-</u> <u>ences_main.html</u>). The next BioMedical Transporters Conference will be held from **August 8-12, 2021** in a Swiss Holiday resort. The conference is being co-organized by NCCR TransCure.

SLC mini-review series and BioParadigms website

There are currently 65 human transporter gene families belonging to the SLC (solute carrier) series and these families include 432 genes. Matthias Hediger serves as Special Advisor on SLCs to the HUGO Gene Nomenclature Committee (HGNC). The SLC tables are presented on the BioParadigms website (<u>http://www.biopara-digms.org/slc/intro.htm</u>).

Research output, past 5 years – Matthias A. Hediger

Link to website showing complete list of publications:

https://www.ncbi.nlm.nih.gov/pubmed/?term=Hediger%20MA *) Co-Corresponding author

1) Publications in international peer-reviewed scientific journals

*) Co-Corresponding author

- 1. Manatschal1 C, Pujol-Giménez, J, Poirier M, Reymond JL, **Hediger MA**, Dutzler R. Mechanistic basis of the inhibition of SLC11/NRAMP-mediated metal 1 ion transport by aromatic bis-isothiourea substituted compounds. *eLife*. 2019, in press.
- 2. Cunha MR, Bhardwaj R, Lindinger S, Butorac C, Romanin C, **Hediger MA**^{*}, Reymond JL. Photoswitchable Inhibitor of the Calcium Channel TRPV6. *ACS Med Chem Lett.* 2019;**10**:341-1345.
- 3. Lüscher BP, Surbek DV, Clémençon B, Huang X, Albrecht C, Marini C, **Hediger MA**, Baumann MU. Different Pharmacological Properties of GLUT9a and GLUT9b: Potential Implications in Preeclampsia. *Cell Physiol Biochem*. 2019;**53**:508-517.
- 4. Pereira GJV, Tavares MT, Azevedo RA, Martins BB, Cunha MR, Bhardwaj R, Cury Y, Zambelli VO, Barbosa EG, **Hediger MA**, Parise-Filho R. Capsaicin-like analogue induced selective apoptosis in A2058 melanoma cells: Design, synthesis and molecular modeling. *Bioorg Med Chem*. 2019;**27**:2893-2904.
- Stergachis AB, Pujol-Giménez J, Gyimesi G, Fuster D, Albano G, Troxler M, Picker J, Rosenberg PA, Bergin A, Peters J, El Achkar CM, Harini C, Manzi S, Rotenberg A, Hediger MA^{*}, Rodan LH. Recurrent SLC1A2 variants cause epilepsy via a dominant negative mechanism. *Ann Neurol.* 2019;85:921-926.
- 6. Gyimesi G, Albano G, Fuster DG, **Hediger MA**^{*)} and Pujol-Giménez J. Unraveling the structural elements of pH sensitivity and substrate binding in the human zinc transporter SLC39A2 (ZIP2). *J Biol Chem.* 2019;**294**:8046-8063.
- 7. Butorac C, Muik M, Derler I, Stadlbauer M, Lunz V, Krizova A, Lindinger S, Schober R, Frischauf I, Bhardwaj R, **Hediger MA**, Groschner K, Romanin C. A novel STIM1-Orai1 gating interface essential for CRAC channel activation. *Cell Calcium*. 2019;**79**:57-67.
- 8. Bulla M, Gyimesi G, Kim JH, Bhardwaj R, **Hediger MA**, Frieden M, Demaurex N. ORAI1 channel gating and selectivity is differentially altered by natural mutations in the first or third transmembrane domain. *J Physiol* 2019;**597**:561-582.
- Franz MC, Pujol-Gimenez J, Montalbetti N, Fernandez-Tenorio M, DeGrado TR, Niggli E, Romero MF, Hediger MA. Reassessment of the transport mechanism of the human zinc transporter SLC39A2. *Biochemistry* 2018;57:3976-3986.
- 10. Kandasamy P, Gyimesi G, Kanai Y, **Hediger MA**. Amino acid transporters revisited: New views in health and disease *Trends Biochem Sci.* 2018;**43**:752-789

- 11. Clémençon B, Lüscher BP, **Hediger MA**. Establishment of a novel microscale thermosphoresis ligand-binding assay for characterization of SLC solute carriers using oligopeptide transporter PepT1 (SLC15 family) as a model system. *J Pharmacol Toxicol Methods* 2018;**92**:67-76.
- 12. Pujol-Giménez J, **Hediger MA**^{*}, Gyimesi G. A novel proton transfer mechanism in the SLC11 family of divalent metal ion transporters. *Sci Rep.* 2017;**7**:6194.
- 13. Dalghi MG, Ferreira-Gomes M, Montalbetti N, Simonin A, Strehler EE, **Hediger MA**, Rossi JP. Cortical cytoskeleton dynamics regulates plasma membrane calcium ATPase isoform-2 (PMCA2) activity. *Biochim Biophys Acta*. 2017;**1864**:1413-1424.
- Lüscher BP, Marini C, Jorger-Messerli M, Huang X, Hediger MA, Albrecht C, Baumann MU, Surbek DV. Placental glucose transporter (GLUT)-1 is down-regulated in preeclampsia. *Placenta* 2017;55:94-99
- 15. Bhardwaj R, **Hediger MA**, Demaurex N. Redox modulation of STIM-ORAI signaling. *Cell Calcium*. 2016;**60**:142-52.
- 16. Clémençon B, Fine M, **Hediger MA**. Conservation of the oligomeric state of native VDAC1 in detergent micelles. *Biochimie*. 2016;**127**:163-72.
- 17. Leuenberger M, Ritler A, Simonin A, **Hediger MA**, Lochner M. Concise Asymmetric Synthesis and Pharmacological Characterization of All Stereoisomers of Glutamate Transporter Inhibitor TFB-TBOA and Synthesis of EAAT Photoaffinity Probes. *ACS Chem Neurosci.* 2016;**7**:534-9.
- Dhayat N, Simonin A, Anderegg M, Pathare G, Lüscher BP, Deisl C, Albano G, Mordasini D, Hediger MA, Surbek DV, Vogt B, Sass JO, Kloeckener-Gruissem B, Fuster DG. Mutation in the Monocarboxylate Transporter 12 Gene Affects Guanidinoacetate Excretion but Does Not Cause Glucosuria. J Am Soc Nephrol. 2016;27:1426-36.
- 19. Simonin A, Montalbetti N, Gyimesi G, Pujol-Giménez J, **Hediger MA**. The Hydroxyl Side Chain of a Highly Conserved Serine Residue Is Required for Cation Selectivity and Substrate Transport in the Glial Glutamate Transporter GLT-1/SLC1A2. *J Biol Chem.* 2015;**290**:30464-74.
- 20. Simonin C, Awale M, Brand M, van Deursen R, Schwartz J, Fine M, Kovacs G, Häfliger P, Gyimesi G, Sithampari A, Charles RP, Hediger MA, Reymond JL. Optimization of TRPV6 Calcium Channel Inhibitors Using a 3D Ligand-Based Virtual Screening Method. *Angew Chem Int Ed Engl.* 2015;54:14748-52.
- 21. César-Razquin A, Snijder B, Frappier-Brinton T, Isserlin R, Gyimesi G, Bai X, Reithmeier RA, Hepworth D, **Hediger MA**^{*)}, Edwards AM, Superti-Furga G. A Call for Systematic Research on Solute Carriers. *Cell*. 2015;**162**:478-87.
- 22. Damseh N, Simonin A, Jalas C, Picoraro JA, Shaag A, Cho MT, Yaacov B, Juusola J, Al-Ashhab M, Bale S, Telegrafi A, Retterer K, Pappas JG, Cappell J, Yeboa KA, Abu-Libdeh B, Hediger MA, Chung WK, Elpeleg O, Edvardson S. Mutations in SLC1A4, encoding the brain serine transporter, associated with developmental delay, microcephaly and hypomyelination. *J Med Genet*. 2015;52:541-7.
- 23. Montalbetti N, Simonin A, Simonin C, Awale M, Reymond JL, **Hediger MA**. Discovery and characterization of a novel non-competitive inhibitor of the divalent metal transporter DMT1/SLC11A2 *Biochem Pharmacol.* 2015;**96**:216-24.
- 24. Clémençon B, Fine M, Schneider P, **Hediger MA.** Rapid method to express and purify human membrane protein using the Xenopus oocyte system for functional and low-resolution structural analysis. *Methods Enzymol.* 2015;**556**:241-65.
- 25. Clémençon B, Lüscher BP, Fine M, Baumann MU, Surbek DV, Bonny O, **Hediger MA**. Expression, purification, and structural insights for the human uric acid transporter, GLUT9 using the Xenopus laevis oocytes system. *PLoS ONE*. 2014;**9**:e108852.
- 26. Franz MC, Simonin A, Graeter S, **Hediger MA**, Kovacs G. Development of the first fluorescence screening assay for SLC39A2 zinc transporter. *J Biomol Screen*. 2014;**19**:909-16.

- 27. Montalbetti N, Simonin A, Dalghi MG, Kovács G, **Hediger MA**. Development and validation of a fast and homogeneous cell-based fluorescence screening assay for divalent metal transporter-1 (DMT1/SLC11A2) using the FLIPR tetra. *J Biomol Screen*. 2014;**19**:900-8.
- 28. Clémençon B, Fine M, Lüscher B, Baumann MU, Surbek DV, Abriel H, **Hediger MA**. Expression, purification, and projection structure by single particle electron microscopy of functional human TRPM4 heterologously expressed in Xenopus laevis oocytes. *Protein Expr Purif.* 2014;**95**:169-76.
- 29. Marini C, Lüscher BP, Jorger-Messerli M, Sager R, Huang X, Gertsch J, **Hediger MA**, Albrecht C, Baumann MU, Surbek DV. Placental Glucose Transporter (GLUT1) expression in pre-eclampsia. *Reprod Sci.* 2014;**21**:1A-70A.
- 30. Jain A, Schneider H, Aliyev E, Soydemir F, Baumann M, Surbek D, **Hediger MA**, Brownbill P, Albrecht C. Hypoxic treatment of human dual placental perfusion induces a pre-eclampsia-like inflammatory response. *Lab Invest.* 2014;**94**:873-80.
- 31. Montalbetti N, Dalghi MG, Albrecht C, Hediger MA. Nutrient transport in the mammary gland: calcium, trace minerals and water soluble vitamins. J Mammary Gland Biol Neoplasia. 2014;19:73-90.

2) Peer-reviewed books/monographs - N/A

3) Peer-reviewed conference papers

• Lüscher BP, Clémençon B, Marini C, Huang X, Sager R, Jeanneret C, Reymond J-L, Albrecht C, Hediger MA, Surbek DV, Baumann MC, Placental uric acid transport system: Glucose Transporter 9 (SLC2A9). Reprod Sci. 2014;21:1A-70A.

4) Contributions to books

• Peng, J-B, Suzuki Y, Gyimesi, G and **Hediger MA.** TRPV5 and TRPV6 calcium-selective channels. In: Juliusz Ashot Kozak, James W. Putney, Jr., editors. Calcium Entry Channels in Non-Excitable Cells. CRC Press/Taylor & Francis; 2018; Chapter 13; p241-274.

5) Patents and licenses

Methods of altering calcium transport (TRPV6)

• Patent number: 7078178 (USPTO)

Abstract: Methods of altering transmembrane calcium transport by altering expression of a calciumtransport protein are described.

Type: Grant Filed: April 22, 2003 Date of Patent: July 18, 2006 Inventors: Matthias A. Hediger, Edward M. Brown, Ji-Bin Peng

• Methods for transporting vitamin C (SLC23 family)

Patent number: 7371536 (USPTO) Abstract: The invention provides methods for regulating the transport of vitamin C across membranes.

Type: Grant Filed: April 7, 2003 Date of Patent: May 13, 2008 Inventor: Matthias A. Hediger

6) Oral contributions to international conferences

- 2019 Plenary speaker: Fundamentals and importance of the SLC solute carrier superfamily and future perspectives. 60th Congress of the Italian Society of Biochemistry and Molecular Biology (SIB), Lecce, Italy.
- 2019 Opening remarks and overview of the diversity of human membrane transporters and ion channels: BioMedical Transporters 2019, Membrane transporters and channels: From basic research to drug development and clinical application. 11th international research conference, Lucerne, Switzerland.
- 2018 Plenary Speaker: Current vision and future direction of transporter research. International Meeting on 22nd MDO and 33rd JSSX "Societal impact of ADME/Tox research on safety & toxicity of drug products", October 1 to 5, 2018, Kanazawa, Japan.
- 2018 Invited Speaker: Future perspectives of transporter research. End of Phase II NCCR TransCure Symposium. University of Bern, Switzerland.
- 2017 Opening remarks: BioMedical Transporters 2017, SLC and ABC transporters and ion channels in drug discovery and preclinical development. 10th international research conference, Lausanne, Switzerland.
- 2016 Invited speaker: Solute Carrier Proteins: Unlocking the Gene-Family for Effective Therapies. Symposium of the New York Academy of Sciences, USA.
- 2015 Opening presentation: BioMedical Transporters 2015, Membrane transporters From basic science to drug discovery. 9th international research conference, Lugano, Switzerland.
- 2014 Invited speaker: Fundamentals of the SLC series. SLC Workshop, Vienna, Organized by Giulio Superti Furga.

7. Outreach activities

- Exhibition by NCCR TransCure at a recent two day annual commercial Bernese spring fair, called BEA. Explaining children and young students how to use a pipette, how to look through a microscope and what the basic goals of NCCR TransCure are about. Presenting a video showing Trans-Cure's automated screening technologies was presented.
- Press release, June 2018, Media Relations, University of Bern. Topic: The new Swiss SNF-funded Sinergia Project entitled "*The role of mitochondrial carriers in metabolic tuning and reprogramming by calcium flow across membrane contact sites*", awarded to Matthias Hediger (Coordinator), Martin Lochner and Inti Zlobec (University of Bern), Edmund Kunji (University of Cambridge, UK) and Nicolas Demaurex (University of Geneva).
- Various other press releases in connection with NCCR TransCure discoveries; latest public outreach available via Twitter: <u>https://twitter.com/NCCR_TransCure</u>

8. General contributions to science

- Founder of the National Center of Competence in Research, called NCCR TransCure (years 2010 to 2022)
- Founder of the International Post-Doctoral Fellowship Program "IFP TransCure", supported by the FP7 European Marie Curie Actions Grant (years 2012 to 2018).

9. Other contributions

The **BioParadigms SLC** (Solute Carrier) gene tables (<u>https://www.bioparadigms.org/</u>) provide a versatile scientific resource, showing the latest up-to-date information on all approved SLC families and their members, as well as relevant links to gene databases and reviews in the literature. The original version of the SLC tables was generated by the authors of the 2004 SLC reviews in Pflügers Archives. The newly revised tables have been generated by the authors of the 2013 reviews, which

have been published in the Journal Molecular Aspects of Medicine. The details regarding these two review series are as follows:

- Guest Editor, special issue "The ABCs of membrane transporters in health and disease (SLC series); Molecular Aspects of Medicine, Volume 34, Issues 2-3, April/June 2013 (*total of 50 reviews on SLC solute carrier families*).
- Guest Editor, special issue "Membrane Transporters: Solute Carriers" (total of 51 reviews on SLC solute carrier families).
- Guest Edited by Prof Matthias A. Hediger & Dr David Hepworth (Pfizer); *Med. Chem. Comm.* (Royal Society of Chemistry), Volume 7, 2016. *This collection of articles is a celebration of all areas of research where the chemical sciences have impacted the study of the SLC solute carrier superfamily.*