## Curriculum Vitae – Prof. Dr. med. Raphael Guzman



### 1) Personal Information

First Name:	Raphael	
Last Name: Address:	Guzman University Hospital Basel, Dept. of Neurosurgery, Spitalstrasse 21,	Scopus Full CV
	4031 Basel Phone: +41 61 3287522	
E-mail:	raphael.guzman@unibas.ch, raphael.guzman@usb.ch	
Webpage:	https://www.unispital-basel.ch/ueber-uns/departemente/kopforgane-wirbelsaeulen-u	<u>und-</u>
	neuromedizin/kliniken/neurochirurgie/ueber-uns/team/pers/raphael-guzman/	
	https://biomedizin.unibas.ch/en/research/research-groups/guzmann-lab/	
	https://www.ukbb.ch/de/personal/personen/Guzman-Raphael.php	

### 2) Education

1986 - 1991 1991 - 1997	College, Business and Administration, Bern, Switzerland Medical School, University of Bern, Bern, Switzerland
1997 – 1998	Research Doctoral Student
1998	Swiss federal examination in Medicine
1998	M.D. Degree University of Bern, Bern, Switzerland, 12/03/1998
1998 – 2004	Neurosurgical residency, Dept. of Neurosurgery, University of
	Bern, Switzerland
2004 - 2006	Postdoctoral research fellowship, stroke regenerative medicine, Stanford University
2007	Neurosurgery Board Certification (European Union and Switzerland)
2005 - 2007	Cerebrovascular and Pediatric Neurosurgery Fellowship, Stanford University, School of
	Medicine; Department of Neurosurgery

### 3) Employment history

1998 – 2004	Neurosurgical Resident, University Hospital Bern
2004 - 2006	Postdoctoral research fellowship, stroke regenerative medicine, Stanford University
2005 - 2007	Cerebrovascular and Pediatric Neurosurgery Fellowship, Stanford University, School of
	Medicine; Department of Neurosurgery
2007 – 2012	Assistant Professor, Dept. of Pediatric Neurosurgery, Stanford University
2012 – 2021	Vice Chairman, Dept. of Neurosurgery, University Hospital Basel
2021 - present	Chairman, Dept. of Neurosurgery, University Hospital Basel

### 4) Institutional responsibilities and Governing Activities

2012 – present	Group Leader - Brain Ischemia and Regeneration, Dept. of Biomedicine, University Hospital Basel
2015 - present	Steering Committee Stroke Center, University Hospital Basel
2016 – present	Steering committee Basel Stem Cell Network (BSCN)
2016 – present	University of Basel Academic Promotions Commission
2017 - present	President Basel Clinical Neuroscience
	Network
2017 - present	Steering Committee Neuroscience Network Basel (NNB)
2020-present	President of the Swiss Society of Neurosurgery
2021 - present	Executive Board Department of Biomedical Engineering
2021 – present	Chief Pediatric Neurosurgery, University Children's
-	Hospital Basel
2021 – present	Chief cerebrovascular Neurosurgery, University
	Hospital Basel

### 5) Approved research projects and Grant Support (last 5 years)

- 6/2013 5/2017 Swiss National Science Foundation, CHF 300'960 Title: Therapeutic Relevance of stem cells for white matter regeneration in neonatal hypoxiaischemia.
  4/2015 – 3/2019 Swiss National Science Foundation, CHF 349'422
- 4/2015 3/2019 Swiss National Science Foundation, CHF 349'422 Title: Characterization of Telomerase-mediated regulation of EGFR- and BMP/SMADsignaling essential for proliferation and invasion in human brain tumors

10/2015 – 9/2018	Swiss National Science Foundation, CHF 372'000 Title: Cold-inducible RBM3 in neuroprotection and neurogenesis.	
7/2016-6/2019	Department of Surgery University of Basel, CHF 600'000 Title: Bioengeneering of scaffolds and matrix for central and peripheral nervous system	
7/2017-6/2018	regeneration. Novartis Innovation Fund, CHF 60'000	
	Title: Enhancement of oligodendrogenesis is indirectly mediated through the neural stem cell secretome.	
11/2017 – 10/2020Komission für Technologie und Innovation (KTI, 27395.1 PFLS-LS), CHF 800'000 Title: Brain Shift Compensation		
8/2019 – 7/2021	Gerbert Rüf Foundation (GRS-058/18), CHF 695'000 Titel: Nano engineered neural interfaces to treat Alzheimer's disease	
4/2022 - 3/2023	Bangerter Rhyner Stiftung, CHF 80'000 Title: Neurogenese -Biomarker im Liquor von pädiatrischen Patienten	

## 6) Supervision of junior researchers (past 3 years out of 24 candidates in the USA and Switzerland)

Stephan Moser, **MSc 2015** Kyrill Karli, **BS 2015** Urs Fish MD, **PhD 2017** Ashesh Shah, **PhD 2018** Mehrdad Ahmadi, **PhD 2020** Hervé Nguendo **PhD 2020** Alois Hopf, **PhD cand. 2022** Nilabh Gosh, **PhD cand. 2022** Tim Jonas Hallenberger, **MD PhD cand. 2024** 

### 7) Teaching activities

2007 – 2012PhD Supervision, Research Committees and regular lectures, Stanford University2012 – presentRegular lectures, clinical skill training and bedside training, University of Basel

# 8) Scientific Reviewing for national granting agencies and Journals, Scientific Advisory Boards

Swiss National Science Foundation (SNSF), Association Nationale de Recherche (ANR), Medical Research Council (MRC)

### Scientific Reviewer (Journals 2004-present)

Annals of Neurology, Cerebrovascular Diseases, Journal of Neuroscience Research, Journal of Neurosurgery, Journal of Neurosurgery Peds, Journal of Cerebral Blood Flow and Metabolism, Neurobiology of Disease, Neuroscience Letters, Neurosurgery, Stroke, Science Translational Medicine, PNAS, Plos One, Childs Nervous System, World Neurosurgery

#### **Editorial Board**

Pediatric Neurosurgery, Clinical and Translational Neuroscience, International Vascular Medicine, Recent Patents on Regenerative Medicine

### Scientific Advisory Boards and Consultant

BottNeuro (Co-Founder, Scientific Advisor), Apeiron life (Scientific Advisor), Temple Therapeutics (Scientific Advisor), Leica (Consultant), AdeTherapeutics Inc (Scientific Advisor past), StemCells Inc. (Consultant, past), Branchpoint Technologies (Scientific Advisor past), Cliniscient (Scientific Advisor past), XBio (Consultant past), Idorsia (Consultant past)

### 9) Society Memberships

Society for Neuroscience, American Association of Neurological Surgeons (AANS), Congress of Neurological Surgeons (CNS), AANS/CNS Joint Cerebrovascular Section, AANS/CNS Joint Pediatric Section, American Society for Pediatric Neurosurgery, European Society of Pediatric Neurosurgery, Swiss Federation of Clinical Neurosciences (SFCNS).

### 10) Organization of conferences

**Stem Cell Conference Basel 2018:** StemCell dynamics throughout life: from development to adult. 29.-31.8.2018

Pediatric Neurosurgery Symposium: 2017, 2018, 2019, 2021, 2022 Stroke Center Symposium: 2017, 2018, 2019,2021

Basel, 20.05.2022

## Major scientific achievements of Prof. Dr. med. Raphael Guzman

**Contributions to Science (1)** | As a clinician I have been especially interested in doing translational and clinical research to potentially develop novel therapies for patients in need. My interest in hemorrhagic and ischemic stroke has led to over 100 publications on preclinical and clinical topics related to stroke. Hemorrhagic stroke particularly remains an unsolved therapeutic challenge. Early in my career I investigated the imaging characteristics of brain hemorrhage in CT and Magnetic resonance imaging, which started to offer more sophisticated sequences to differentiate time and etiology of brain hemorrhage [1]. There always was a lack of preclinical models for intracerebral hemorrhage (ICH) and hence we developed an experimental ICH rodent model that helped us study the pathophysiology and imaging characteristics after a brain hemorrhage [2]. One of the goals was to develop neuroprotective and neuroregenerative strategies [3]. The newest clinical literature clearly supports the concept of early minimally invasive hemorrhage evacuation, which is the basis of the current proposal. Additionally, over the years I have been involved in many clinical studies related to brain hemorrhage, most prominently the swiss subarachnoidal hemorrhage study (SOS), where I am part of the scientific advisory board [4]

[1]: El-Koussy M, **Guzman R**, Bassetti C, Stepper F, Barth A, Lövblad KO, Schroth G. CT and MRI in acute hemorrhagic stroke. Cerebrovasc Dis. 2000 Nov-Dec;10(6):480-2. doi: 10.1159/000016113. PMID: 11070382.

[2]: Barth A, **Guzman R**, Andres RH, Mordasini P, Barth L, Widmer HR. Experimental intracerebral hematoma in the rat. Restor Neurol Neurosci. 2007;25(1):1-7. PMID: 17473390.

[3]: Andres RH, **Guzman R**, Ducray AD, Mordasini P, Gera A, Barth A, Widmer HR, Steinberg GK. Cell replacement therapy for intracerebral hemorrhage. Neurosurg Focus. 2008;24(3-4):E16. doi: 10.3171/FOC/2008/24/3-4/E15. PMID: 18341392.

[4]: Roethlisberger M, Achermann R, Bawarjan S, Stienen MN, Fung C, D'Alonzo D, Maldaner N, Ferrari A, Corniola MV, Schöni D, Valsecchi D, Maduri R, Seule MA, Burkhardt JK, Marbacher S, Bijlenga P, Blackham KA, Bucher HC, Mariani L, **Guzman R**, Zumofen DW; Swiss SOS Study Group. Predictors of Occurrence and Anatomic Distribution of Multiple Aneurysms in Patients with Aneurysmal Subarachnoid Hemorrhage. World Neurosurg. 2018 Mar;111:e199-e205. doi: 10.1016/j.wneu.2017.12.046. Epub 2017 Dec 16. PMID: 29258940.

**Contributions to Science (2)** | One of the most potent neuroprotective measures currently available in clinical practice is hypothermia. For instance, hypothermia is the only approved acute neuroprotective treatment for newborns with hemorrhagic or ischemic stroke. We have studied the molecular basis of neuroprotection of hypothermia. We describe the role of RBM3, a cold-induced RNA binding protein involved in mRNA biogenesis RBM3 [1,2]. Another area of interest in hemorrhagic and ischemic stroke is neuroinflammation. Microglia are a distinct cellular component originating from the yolk sac and populating the brain during embryogenesis. The understanding of microglia was initially restricted to its function as the brains immune cells but in the last decade the relevance of microglia for brain development, brain homeostasis, neuroregeneration and neurodegeneration was highlighted. We have specifically contributed to the better understanding of microglia in the neurogenic niche in neural development where we find region and time specific characteristics of microglia morphologically and at the gene expression level [3]. We also described critical changes of microglia after ischemia and its relation to functional recovery [4]. Finally, we described the critical interplay between microglia and neural stem cells in the neurogenic niche in the mature rodent brain [5].

[1] Zhu, X., Yan, J., Bregere, C., Zelmer, A., Goerne, T., Kapfhammer, J. P., **Guzman, R**., & Wellmann, S. (2019). RBM3 promotes neurogenesis in a niche-dependent manner via IMP2-IGF2 signaling pathway after hypoxic-ischemic brain injury. Nature Communications,10(1). https://doi.org/10.1038/s41467-019-11870-x.

[2] Yan, J., Goerne, T., Zelmer, A., **Guzman, R.,** Kapfhammer, J. P., Wellmann, S., & Zhu, X. (2019). The RNA-Binding Protein RBM3 Promotes Neural Stem Cell (NSC) Proliferation Under Hypoxia. Frontiers in Cell and Developmental Biology,7. https://doi.org/10.3389/fcell.2019.00288.

[3] Fisch, U., Brégère, C., Geier, F., Chicha, L., & **Guzman, R**. (2020). Neonatal hypoxia-ischemia in rat elicits a regionspecific neurotrophic response in SVZ microglia. Journal of Neuroinflammation,17(1). https://doi.org/10.1186/s12974-020-1706-y.

[4] Lartey, F. M., Ahn, G.-O., Ali, R., Rosenblum, S., Miao, Z., Arksey, N., Shen, B., Colomer, M. V., Rafat, M., Liu, H., Alejandre-Alcazar, M. A., Chen, J. W., Palmer, T., Chin, F. T., **Guzman, R**., Loo, B. W., Jr., & Graves, E. (2014). The Relationship Between Serial [18 F]PBR06 PET Imaging of Microglial Activation and Motor Function Following Stroke in Mice.Molecular Imaging and Biology,16(6), 821–829. https://doi.org/10.1007/s11307-014-0745-0.

[5] Mosher, K. I., Andres, R. H., Fukuhara, T., Bieri, G., Hasegawa-Moriyama, M., He, Y., **Guzman, R.**, & Wyss-Coray, T. (2012). Neural progenitor cells regulate microglia functions and activity. Nature Neuroscience,15(11), 1485–1487. https://doi.org/10.1038/nn.3233.

**Contributions to Science (3)** | My work on neural stem cell biology and its application for neuroregeneration in the past 20 years has culminated in a clinical cell transplantation trial for patients with spinal cord injury [1]. I am on a scientific advisory panel with the Christopher Reeves Foundation to develop a new roadmap defining critical steps in the development of novel therapy for spinal cord injured patients. While this is not the topic of the current proposal, it highlights the paths that I would like to go with my research. Also for stroke I have led paths that should hopefully led to clinical translation. As part of an international scientific expert group appointed by the National Institute of Health (NIH) we have defined targets and guidelines for the research and implementation of cellular therapies for patients with ischemic brain injuries [2]. As part of these guidelines, I have significantly contributed to the development of techniques for intravascular systemic cell delivery to treat stroke with original contributions [3] and reviews of this topic [4].

[1] Levi, A. D., Okonkwo, D. O., Park, P., Jenkins, A. L., III, Kurpad, S. N., Parr, A. M., Ganju, A., Aarabi, B., Kim, D., Casha, S., Fehlings, M. G., Harrop, J. S., Anderson, K. D., Gage, A., Hsieh, J., Huhn, S., Curt, A., & **Guzman, R**. (2017). Emerging Safety of Intramedullary Transplantation of Human Neural Stem Cells in Chronic Cervical and Thoracic Spinal Cord Injury.Neurosurgery,82(4), 562–575. https://doi.org/10.1093/neuros/nyx250.

[2] Savitz, S. I., Cramer, S. C., Wechsler, L., Aronowski, J., Boltze, J., Borlongan, C., Case, C., Chase, T., Chopp, M., Carmichael, S. T., Cramer, S. C., Duncan, P., Finklestein, S., Fischkoff, S., **Guzman, R**., Hess, D. C., Huang, D., Hinson, J., Kautz, S. (2014). Stem Cells as an Emerging Paradigm in Stroke 3. Stroke,45(2), 634–639. https://doi.org/10.1161/strokeaha.113.003379.

[3] Andres, R. H., Choi, R., Pendharkar, A. V., Gaeta, X., Wang, N., Nathan, J. K., Chua, J. Y., Lee, S. W., Palmer, T. D., Steinberg, G. K., & **Guzman, R**. (2011). The CCR2/CCL2 Interaction Mediates the Transendothelial Recruitment of Intravascularly Delivered Neural Stem Cells to the Ischemic Brain.Stroke,42(10), 2923–2931. https://doi.org/10.1161/strokeaha.110.606368.

[4] Guzman R, Janowski M, Walczak P. Intra-Arterial Delivery of Cell Therapies for Stroke. Stroke. 2018 May;49(5):1075-1082. doi: 10.1161/STROKEAHA.117.018288. Epub 2018 Apr 18. PMID: 29669876; PMCID: PMC6027638.