BIOGRAPHICAL SKETCH

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NAME: Aguzzi, Adriano

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Director and Full Professor, Institute of Neuropathology University of Zurich

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Medical School, University of Freiburg (D).	MD	1980-86	
Internship in Basel (CH) and Freiburg (D).			
Columbia University, New York (Dept. of Pathology).		1983	
Foreign medical graduates Examination		1985	
in the Medical Sciences USA (ECFMG).			
University Hospital of Zürich, CH.		1986-89	Neuropathology
Institute of Molecular Pathology, Vienna, A		1989-92	

A. Personal Statement

The primary mission of my lab is to develop mammalian models of human disease, from which we then extract general pathogenetic principles. While we have historically focused on prion diseases, we also study further neurological and, occasionally, extraneural diseases if our discoveries take us there. Our work is mostly precompetitive and focuses on the molecular triggers of organ dysfunction. While we occasionally develop commercially exploitable reagents (e.g. antibodies) and file patent applications, we feel that downstream activities (e.g. drug discovery; diagnostic test development) do not belong to our core competence and are best passed on to our industrial partners.

B. Positions and Honors

Positions and Employment

1993 Consultant (Oberarzt), and Lecturer (Privat-Dozent) in Pathology and Neuropathology, Univ. of Zürich
1995- Director of the Swiss National Reference Center for Prion Diseases
1997- Ordinarius (Full Professor) of Neuropathology and Director of the Institute of Neuropathology, University of Zürich.
1998- Joint Professorship (Neuropathology) of the Medical Faculty and Faculty of Natural Sciences, University of Zurich.
2004 Chairman, Department of Pathology, University Hospital of Zurich

Other Experience and Professional Memberships

1998 Swiss Society of Neuropathology (President: 1998-2002)
1998 EMBO Member (European Molecular Biology Organization)
1996 Royal College of Pathology (MRCPath) and German Society of Neuropathology
1999 International Society of Neurovirology (Member of the Board of Directors)
1997 International Society of Neuropathology (Councilor 1997-99)
1997 SEAC (Spongiform Encephalopathy Advisory Committee, UK)
2000 Swiss Academy of the Medical Sciences (SAMW): individual member
2001 Deutsche Akademie der Naturforscher Leopoldina
2002 Fellow of the Royal College of Physicians of London (FRCP)

Honors

1995 Ernst Th. Jucker Prize, Zürich
1997 Pfizer Award for Neurobiology, Zürich
1998 EMBO Gold Medal of the European Molecular Biology Organization, Lisbon
1998 Cloëtta Award, Zürich
1999 Ernst-Jung Prize for Medicine, Hamburg
2000 Aschoff Medal, Freiburg
2000 Biotec Award, Milano
2001 German Academy of Science (Leopoldina) Prize, Halle
2001 Medal of the Royal Swedish Academy of Medicine, Stockholm
2001 ICAAC Award and Lecture, Chicago
2002 Doctor medicinae honoris causa, University of Liège

C. Contribution to Science

I have devoted the past 20 years to studying the immunological and molecular basis of prion pathogenesis. Combining transgenetics with molecular and immunological techniques, I have aimed to clarify the pathogenesis of the disease, and to identify cells and molecules involved in prion neuroinvasion.

The discovery of pervasive colonization of the immune system by prions has convinced most of the world's governments to undertake efforts to limit the exposure of humans to prions derived from farm animals. As further crucial practical consequence of my discoveries, the UK government has started, in the year 1998, universal mandatory leukodepletion of donated blood units. This measure was very controversial at the time, but it has probably saved many lives, since not a single case of blood-borne transmission of Creutzfeldt-Jakob disease was recorded in recipients of UK blood after its introduction.

My discovery that chronic inflammation controls the organ tropism of prion diseases has crucially contributed to clarifying how scrapie transmits horizontally within sheep flocks – a question that had been controversially discussed since the late 19th century. The realization that prion excretion necessitates inflammation of the excretory organ as a cofactor in addition to prion infection will pave the way to effective strategies for the eradication of prion diseases from small ruminants.

My work on microglia was seminal to establish that microglia is helpful, rather than detrimental, in fighting prion diseases. Using original models of conditional lineage ablation, I have shown that the removal of microglia greatly accelerates prion disease. This discovery has a fundamental impact on therapeutic strategies against aggregation proteinopathies, and clearly indicates that the innate immunity provided by microglia is important and should be facilitated.

Finally, my work related to the histogenesis of follicular dendritic cells, which spans over a decade and has culminated in a recent Cell paper, has clarified how ectopic lymphoid organs can arise anywhere the body following chronic inflammatory stimuli. This discovery has profound consequences for our understanding of the factors controlling chronic inflammation and autoimmunity.

Selected publications (in chronological order)

1. Brandner S, Isenmann S, Raeber A, Fischer M, Sailer A, Kobayashi Y, Marino S, Weissmann C, and Aguzzi A. (1996). Normal host prion protein necessary for scrapie-induced neurotoxicity. Nature 379:339-343.
2. Blättler T, Brandner S, Raeber A.J, Klein M.A, Voigtländer T, Weissmann C, and Aguzzi A. (1997). PrP-expressing tissue required for transfer of scrapie infectivity from spleen to brain. Nature 389:69-73.
3. Klein M.A, Frigg R, Flechsig E, Raeber A.J, Kalinke U, Bluethmann H, Bootz F, Suter M, Zinkernagel R.M, and Aguzzi A. (1997). A crucial role for B cells in neuroinvasive scrapie. Nature 390:687-690.
4. Fischer M.B, Roeckl C, Parizek P, Schwarz H.P, and Aguzzi A. (2000). Binding of disease-associated prion protein to plasminogen. Nature 408:479-483.
5. Klein MA, Kaeser PS, Schwarz P, Weyd H, Xenarios I, Zinkernagel RM, Carroll MC, Verbeek JS, Botto M, Walport MJ, Aguzzi A. (2001). Complement facilitates early prion pathogenesis. Nature Medicine 7:488-492.
6. Heppner FL, Musahl C, Arrighi I, Klein MA, Rulicke T, Oesch B, Zinkernagel RM, Kalinke U, Aguzzi A. (2001). Prevention of Scrapie Pathogenesis by Transgenic Expression of Anti-Prion Protein Antibodies. Science 294:178-182.
7. Glatzel M, Abela E, Maissen M, Aguzzi A. (2003). Extraneural pathologic prion protein in sporadic Creutzfeldt-Jakob disease. New England J Medicine 349:1812-1820.

8. Meier P, Genoud N, Prinz M, Maissen M, Rulicke T, Zurbriggen A, Raeber AJ, Aguzzi A. (2003). Soluble dimeric prion protein binds PrP(Sc) in vivo and antagonizes prion disease. Cell 113:49-60.
9. Prinz M, Heikenwalder M, Junt T, Schwarz P, Glatzel M, Heppner FL, Fu YX, Lipp M, Aguzzi A. (2003). Positioning of follicular dendritic cells within the spleen controls prion neuroinvasion. Nature 425:957-962.
10. Heikenwalder M, Polymenidou M, Junt T, Sigurdson C, Wagner H, Akira S, Zinkernagel R, Aguzzi A. (2004). Lymphoid follicle destruction and immunosuppression after repeated CpG oligodeoxynucleotide administration. Nature Medicine 10:187-192.
11. Heppner FL, Greter M, Marino D, Falsig J, Raivich G, Hovelmeyer N, Waisman A, Rulicke T, Prinz M, Priller J, Aguzzi A. (2005). Experimental autoimmune encephalomyelitis repressed by microglial paralysis. Nature Medicine 11:146-152.
12. Heikenwalder M, Zeller N, Seeger H, Prinz M, Klohn PC, Schwarz P, Ruddle NH, Weissmann C, Aguzzi A. (2005) Chronic lymphocytic inflammation specifies the organ tropism of prions. Science 307:1107-1110.
13. Seeger H, Heikenwalder M, Zeller N, Kranich J, Schwarz P, Gaspert A, Seifert B, Miele G, Aguzzi A. (2005). Coincident scrapie infection and nephritis lead to urinary prion excretion. Science 310:324-326
14. Heikenwalder M, Kurrer M.O, Margalith I, Kranich J, Zeller N, Haybaeck J, Polymenidou M, Matter M, Bremer J, Lindquist SL, Aguzzi A (2008). Lymphotoxin-dependent prion replication in inflammatory stromal cells of granulomas. Immunity 29:998-1008.
15. Krautler NJ, Kana V, Kranich J, Tian Y, Perera D, Lemm D, Schwarz P, Armulik A, Browning JL, Tallquist M, Buch T, Oliveira-Martins JB, Zhu C, Hermann M, Wagner U, Brink R, Heikenwalder M, Aguzzi A. Follicular dendritic cells emerge from ubiquitous perivascular precursors. Cell. 2012 Jul 6;150(1):194-206.
16. Aguzzi A, Falsig J. .Prion propagation, toxicity and degradation. Nature Neurosci. 2012 Jun 26;15(7):936-9. doi: 10.1038/nn.3120.
17. Sonati T, Reimann RR, Falsig J, Baral PK, O'Connor T, Hornemann S, Yaganoglu S, Li B, Herrmann US, Wieland B, Swayampakula M, Rahman MH, Das D, Kav N, Riek R, Liberski PP, James MN, Aguzzi A.The toxicity of antiprion antibodies is mediated by the flexible tail of the prion protein. Nature. 2013 Jul 31. doi: 10.1038/nature12402.
18. Uli S. Herrmann, Anne K. Schütz, Hamid Shirani, Danzhi Huang, Dino Saban, Mario Nuvolone, Bei Li, Boris Ballmer, Andreas K. O. Åslund, Jeffrey J. Mason, Elisabeth Rushing, Herbert Budka1 Sofie Nyström, Per Hammarström, Anja Böckmann, Amedeo Caflisch, Beat H. Meier, K. Peter R. Nilsson, Simone Hornemann, Adriano Aguzzi (2015). Structure-based drug design identifies polythiophenesas antiprion compounds . Science Translational Medicine, 7 (299)

URL to a full list of published work
http://scholar.google.ch/citations?user=3cNp9mgAAAAJ&hl=en&oi=ao

D. Research Support

2015-2020 European Research Council (ERC) Advanced Grant (EUR 2’500’000).
2015-2018 Swiss National Science Foundation (CHF 930’000): “The prion protein in health and disease”
2015-2018 SystemsX.ch (CHF 1'347'224): Systems Biology of Prion diseases” (Coordinator)
2015-2018 E-Rare JTC/Swiss National Science Foundation (CHF 383’603): “Immunotherapy of familial prion diseases” (Coordinator)
2014-2015 Fidelity Biosciences Grant (USD 207’940): “Identification of pathways governing the spread of α-synuclein aggregates” (Coordinator)
2014-2015 Swiss National Science Foundation, R’Equip (CHF 609’632): “High-throughput assays for molecular markers of cytotoxicity”
2013-2016 Swiss National Science Foundation, Sinergia Project (CHF 1'499'779): “Calcium imaging of cellular and circuit dysfunctions in neurodegeneration”
2012-2016 FP7 European Framework Programme (EUR 669’500): Neurinox, “Understanding the role of neuroinflammation in neurodegenerative diseases Understanding the role of neuroinflammation in neurodegenerative diseases”
2010-2015 European Research Council (ERC) Advanced Grant (EUR 2’500’000).
2011-2015 Polish-Swiss Research Programme (PLN 664’376): “Mechanisms of prion neurotoxicity”

2012-2018 Clinical Research Priority Programme, UZH (CHF 1,055,445): “Small RNAs” (coordinator)
2012-2018 Clinical Research Priority Programme, UZH (CHF 987’280): “Human hemato-lymphatic diseases” (partner)
2012-2015 Federal Office of Public Health (CHF 210’000): National Reference Center for Human Prion Diseases.