BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
DO NOT EXCEED FOUR PAGES.

NAME	POSITION TITLE
Flavio Keller	Full Professor of Physiology
	Head, Lab. of Developmental Neuroscience
	University Campus Bio-Medico

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Zurich, Faculty of Medicine	Federal license	10/72-11/78	Medicine
University of Zurich, Faculty of Medicine	Dr. med. (MD)	02/79-10/82	Neuropharmacology
University of Zurich, Faculty of Medicine		1981-1982	Post-graduate course in Experimental Medicine and Biology
University of Zurich, Dept. of Pharmacology	Research Assistant	11/82-07/88	Neuropharmacology
Columbia University, Center for Neurobiology & Behavior, and Howard Hughes Medical Institute	Research Associate	09/88-11/91	Molecular Neurobiology, Synaptic plasticity
University of Zurich, Brain Research Institute (Dr. M.E. Schwab)	Research Associate	01/92-09/93	Developmental Neuroscience

A. Personal Statement

My interest lies in translational research on neurodevelopmental disorders, in particular Autism Spectrum Disorders. I am currently working with a mouse model, the heterozygous reeler mouse, haploinsufficient for Reelin, to assess the interactions between genetic vulnerability, male gender, and environmental factors, leading to cognitive, social, and emotional malfunctioning in adult life. I am also interested in motor development in infants with high risk of autism, especially from the point of view of early diagnosis.

B. Positions and Honors

Positions and Employment

02/79-07/88	Research Assistant, Department of Pharmacology, Faculty of Medicine, University of Zurich
09/88-11/91	Research Associate, Center for Neurobiology and Behavior, Columbia University, and Howard
	Hughes Medical Institute
01/92-09/93	Associate Scientist, University of Zurich, Brain Research Institute.
1994-1997	Lecturer in Neurophysiology, Faculty of Medicine, University of Zurich
09/93-10/02	Associate Professor of Physiology, Università "Campus Biomedico, Roma
11/02-	Full professor of Physiology, Università "Campus Biomedico, Roma

Professional Memberships

2005- Perception-Movement-Action Research Centre (PMARC), University of Edinburgh 2006- Autism Research Consortium, Boston 2009- International Society for Autism Research

<u>Honors</u>

1988-1989 Fellow of the "Stiftung für Medizinisch-Biologische Stipendien" (Basel)

- 1987-1992 Visiting assistant professor, Department of Anatomy, Medical College of Pennsylvania, Philadelphia
- 2002- Visiting Professor of Anthropology, Faculty of Philosophy, Pontifical University of the Holy Cross, Roma, Italy

Editorial Boards

The Open Neuropsychopharmacology Journal, Bentham Publishing Company *Scientifica*, Hindawi Publishing Corporation (Subject Area: Neurology)

C. Selected Peer-reviewed Publications

- Campolo D., Molteni M., Guglielmelli E., Keller F, Laschi C., Dario P. (2006) Towards development of biomechatronic tools for early diagnosis of neurodevelopmental disorders. Conf Proc IEEE Eng Med Biol Soc 1:3242-3245 (PMID 17946557)
- Campolo D, Taffoni F, Schiavone G, Laschi C, Keller F, Guglielmelli E. (2008) A novel technological approach towards the early diagnosis of neurodevelopmental disorders. Conf Proc IEEE Eng Med Biol Soc.2008:4875-4878. (PMID 19163809)
- 3. Laviola G., Ognibene E., Adriani W., Romano E., **Keller F.** (2009) Gene-environment interaction during early development in the heterozygous reeler mouse: Clues for modelling of major neurobehavioral syndromes. **Neuroscience & Biobehavioral Reviews** 33, 560-572.
- 4. Biamonte F., Assenza G., Marino R., D'Amelio M, Panteri R., Caruso D., Scurati S., Garcia Yague J., Garcia-Segura L.M., Cesa R., Strata P., Melcangi R.C., **Keller F.** (2009) Interactions between neuroactive steroids and reelin haploinsufficiency in Purkinje cell survival. **Neurobiology of Disease** 36(1):103-115.
- Halladay AK, Amaral D, Aschner M, Bolivar VJ, Bowman A, Dicicco-Bloom E, Hyman SL, Keller F, Lein P, Pessah I, Restifo L, Threadgill DW (2009) Animal models of autism spectrum disorders: Information for neurotoxicologists. Neurotoxicology 30(5):811-821.
- Taffoni F., Formica D., Campolo D., Keller F., Guglielmelli E: (2009) Block-box instrumented toy: a new platform for assessing spatial cognition in infants. Conf Proc IEEE Eng Med Biol Soc. 2009:210-213 (PMID 19963957)
- 7. Campolo D., Formica D., Guglielmelli E., **Keller F.**, (2010) Kinematic analysis of the human wrist during Pointing Tasks, **Experimental Brain Research** 201(3): 561-573. (PMID 19916007)
- 8. Macrì S., Biamonte F., Romano E., Marino R., **Keller F.,** Laviola G. (2010) Perseverative responding and neuroanatomical alterations in adult heterozygous reeler male mice are mitigated by neonatal estrogen administration. **Psychoneuroendocrinology** 35:1374-1387.
- 9. Schiavone G., Guglielmelli E., Keller F., Zollo L., Chersi F. (2010) A wearable ergonomic gaze-tracker for infants. Conf Proc Eng Med Biol Soc 2010:1283-1286 (PMID 21095919)
- Schiavone G., Formica D., Taffoni F., Campolo D., Guglielmelli E., Keller F. (2011) Multimodal ecological technology: from child's social behavior assessment to child-robot interaction improvement. Int J Soc Robot 3(1): 69-81.
- 11. Campolo D., Taffoni F., Formica D., Schiavone G., **Keller F.**, Guglielmelli E. (2011) Instrumented Toys for Assessing Spatial Cognition in Infants, Frontier in Mechanical Engineering, DOI: 10.1007/s11465-011-0208-0, Online First^a, available online from 2010-12-31.
- 12. Formica D., Campolo D., Taffoni F., **Keller F.**, Guglielmelli E. (2011) Motor adaptation during redundant tasks with the wrist. **Conf Proc IEEE Eng Med Biol Soc.** 2011:4046-4049 (PMID 22255228)
- Campolo D., Taffoni F., Formica D., Schiavone G., Keller F., Guglielmelli E (2011) Inertial-magnetic sensors for assessing spatial cognition in infants. IEEE Tras Biomed Eng 58(5):1499-1503 (PMID 21233040)

14. Campolo D., Taffoni F., Formica D., Iverson J.M., Sparaci L., **Keller F.**, Guglielmelli E. (2011) Embedding inertial-magnetic sensors in everyday objects: Assessing spatial cognition in children, **Journal of integrative Neuroscience** 11(1):103-116.

D. Research Support

Ongoing Research Projects

Italian Ministry of Health (Grant # 2009P9CE2R) Keller (PI) 1/10/2011-30/09/2013 Function of reelin in the amygdalo-hippocampal circuit: structural, electrophysiological and behavioral investigations

This grant aims at modulating Reelin function in the adult mouse hippocampus, using two alternative strategies: a) applicatin or reelin siRNA; b) chronic administration of anti-Reelin monoclonal antibody CR-50. The first approach aims at downregulating Reelin expression, the second one aims to interfere with Reelin function. The resulting new mouse model, characterized by knock-down of Reelin function in the adult hippocampus, will be analyzed by histological, electrophysiological and behavioral methods, focusing on the hippocampus-amygdala circuit.

Autism Speaks (Grant #4919) Keller (PI)

1/10/2008-30/09/2011 (extended to 03/2012)

Analysis of developmental interactions between reelin haploinsufficiency, male sex, and mercury exposure

This grant explores a 3-factor model of neurodevelopmental disease, namely interactions between genetic risk, internal environment (perinatal sex hormone levels) and external environment (mercury exposure) in the heterozygous reeler mouse.

European Union (Grant #231722)Baldassarre (PI)1/05/2009-30/04/2013Intrinsically Motivated Cumulative Learning Versatile Robots (IM-CLeVeR)

This large IP grant involves several robotics, artificial intelligence, development psychology, and primatology labs across Europe, and aims at exploring cumulative and intrinsically motivated learning in children and monkeys, with the aim of developing novel software to enable a highly sophisticated baby-robot (iCub) to autonomously learn simple manipulative tasks such as putting object into holes, learning the correct use of a fork and a knife etc.

Role: Co-I (Role: design and supervision of experiments with children)

R21 HD068584Iverson (PI)4/15/11-4/14/13Sensor-Based Technology in the Study of Motor Skills in Infants at Risk for ASD

The primary goal of this project is to evaluate developmental trajectories and possible developmental delays and impairments in the fine motor skills of infants at heightened (HR) biological risk for ASD, to examine the relation between motor skills and delays exhibited by HR children in other developmental domains, and to provide preliminary information about kinematic and behavioral signatures that may be related to an eventual diagnosis of ASD.

Role: Co-I (Design of experiments with children/supervision of experiments at the Italian site)

Recently Completed Research Support (last 3 years)

European Union (grant #15636) Keller (PI) Thought in Action (TACT)

The goal of this project was to develop novel technologies for unobtrusive monitoring of infant behavior, with the aim of detecting early signs of deviant development.

Autism Speaks (grant #1391)Keller (PI)1/07/2006-31/12/2009Comparative analysis of cerebellar neuropathology in human autistic patients and in cerebellar mouse
mutants.1/07/2006-31/12/2009

The goal of this translational project was to investigate the regional specificity loss of Purkinje cells in postmortem cerebellar specimens of a group of patients with autism in comparison to an age-, sex, and PMImatched control group. In parallel, we analyzed Purkinje cell loss in the newborn heterozygous reeler mouse and its modulation by early administration of neurosteroids.