

# Silvia Zucchelli, Ph.D.

## *Curriculum vitae*

### PERSONAL DATA

First Name: Silvia  
Last Name: ZUCHELLI  
Date and Place of Birth: 28/04/1971 Milan (MI), Italy  
Nationality: Italian

### BIO AND EDUCATION

2001 Ph.D. in Immunology, University of Rome "Tor Vergata", Rome (Italy)  
1995 B.S. in Biological Sciences *cum laude*, University of Milan, Milan (Italy)

### UNIVERSITY CAREER

2013-	Assistant Professor in Genetics, University of Eastern Piedmont, Novara (Italy)
2010-2013	Researcher for Telethon Foundation, SISSA, Trieste (Italy)
2006-2010	Instructor in Neuroscience, SISSA, Trieste (Italy)
2003-2006	Senior Post-doctoral fellow in Neurobiology, SISSA, Trieste (Italy)
2000-2003	Post-doctoral fellow in Immunology, Joslin Diabetes Center, Harvard Medical School, Boston MA (USA)
1996-2000	Studiante di dottorato, IRBM, Merck Research Laboratories, Pomezia, Roma (Italy)
1995-1996	Ph.D. student, IRBM, Department of Biotechnology, Pomezia, Rome (Italy)
1994-1995	Pre-doctoral fellow, IRBM, Department of Biotechnology, Pomezia, Rome (Italy)

### SCIENTIFIC POSITIONS

2011-	Member of the international research consortium FANTOM5 (Functional Annotation of the Mammalian Genome 5), RIKEN, Yokohama (Japan)
2011-	Scientific Advisor of TransSINE Technologies, RIKEN Venture Company, RIKEN, Yokohama (Japan)

### MAIN FIELDS OF INTEREST

1. Functional Genomics of the Brain
2. Long non-coding RNAs

### 3. Neurodegenerative diseases

#### CURRENT ISSUES OF RESEARCH

##### 1. Molecular mechanisms and therapeutic applications of SINEUP technology

We have recently discovered a new class of antisense (AS) lncRNAs, whose dominant effect is to promote translation of partially overlapping sense protein-coding mRNAs with no effects on RNA levels (Carrieri C., et al., Nature 2012). As these lncRNAs depend on an inverted SINEB2 repetitive element for induction of protein synthesis, we named these molecules SINEUPs. SINEUP activity depends on two functional domains: 1) a 5' sequence that overlaps with the coding mRNA in the opposite orientation and that confers target specificity (Binding Domain); 2) an embedded inverted SINEB2 element that functions as activator of translation (Effector Domain) (Zucchelli S., et al., RNA Biology, 2015). We have previously demonstrated that by swapping binding domains it is possible to generate SINEUPs to target virtually any protein of interest (Zucchelli S., Fasolo F., et al., Frontiers in Cellular Neuroscience, 2015; Patrucco L., et al., Gene, 2015). Importantly, the enhancement is within a more physiological range (2-3 fold) than obtained by other gene therapy strategies. These features render SINEUP technology of particular interest for therapeutic correction of haploinsufficiencies (Indrieri A., et al., Scientific Reports, 2016). The aim of our research is to study the molecular mechanisms that control SINEUP activity within the cell and to generate synthetic SINEUPs to target therapeutic proteins and correct haplo-insufficiency defects *in vivo*.

##### 2. Analysis of antisense transcription in *loci* associated to familial forms of neurodegenerative diseases

The FANTOM5 sequencing datasets represent the largest collection of transcriptomes from human cell lines, primary cells and whole tissues of various origins. As part of the FANTOM5 consortium, we contributed to the description of the mammalian promoter expression atlas (Forrest A.R.R., et al., Nature, 2014). The aim of the laboratory is to study antisense transcription at *loci* associated to hereditary forms of neurodegenerative diseases as Alzheimer's disease, Amyotrophic Lateral Sclerosis, Frontotemporal Dementia, Huntington's and Parkinson's disease. Indeed, antisense transcription was validated for a subset of genes, including amyloid precursor protein, microtubule-associated protein tau, DJ-1, leucine-rich repeat kinase 2 and  $\alpha$ -synuclein (Zucchelli S., et al., FANTOM5 satellite manuscript, submitted). Future studies will be focused on the functional role of newly identified antisense transcripts and their impact on neurodegeneration.

#### CURRENT FUNDED PROJECTS

PROGRAMME	FUNDED PROJECT
Programme CARIPO 2014	"THE ROLE OF DNA DAMAGE IN NORMAL BRAIN AGING AND IN PATHOLOGICAL NEURODEGENERATION ASSOCIATED WITH ALZHEIMER'S DISEASE" Rif. 2014-0812)

## TOP FIVE PAPERS

1. Forrest AR, Kawaji H, Rehli M, Baillie JK, de Hoon MJ, Lassmann T, Itoh M, Summers KM, Suzuki H, Daub CO, Kawai J, Heutink P, Hide W, Freeman TC, Lenhard B, Bajic VB, Taylor MS, Makeev VJ, Sandelin A, Hume DA, Carninci P, Hayashizaki Y, **FANTOM Consortium** and the RIKEN PMI and CLST (DGT) **Nature (2014)** Mar 27;507(7493):462-70. (IF 38.597)
2. Carrieri C, Cimatti L, Biagioli M, Beugnet A, **Zucchelli S**, Fedele S, Pesce E, Ferrer I, Collavin L, Santoro C, Forrest AR, Carninci P, Biffo S, Stupka E, Gustincich S. (2012). Long non-coding antisense RNA controls Uchl1 translation through an embedded SINEB2 repeat. **Nature (2012)** 491(7424):454-7 (IF 38.597)
3. Pifferi S, Pascarella G, Boccaccio A, Mazzatenta A, Gustincich S, Menini A, **Zucchelli S**. Bestrophin-2 is a candidate calcium-activated chloride channel involved in olfactory transduction. **Proc Natl Acad Sci USA (2006)** 103(34):12929-34 (IF 9.737)
4. **Zucchelli S.**, Holler P., Yamagata T., Roy M. Benoist C. and Mathis D. "Defective central tolerance induction in NOD mice: genomics and genetics" **Immunity (2005)**; 22: 385-396 (IF 19.266)
5. **Zucchelli S.**, Roccasecca R., Meola A., Bruni Ercole B., Tafi R., Dubuisson J., Galfre' G., Cortese R., and Nicosia A. "Mimotopes of the hepatitis C virus hypervariable region 1, but not the natural sequences, induce cross-reactive antibody response by genetic immunization" **Hepatology (2001)**; 33(3): 692-703 (IF 10.734)

## FURTHER INFORMATION

Silvia Zucchelli is named inventor in the patent "FUNCTIONAL NUCLEIC ACID MOLECULE AND USE THEREOF" USPTO -Serial No. 61/469,399.