

CV Prof. Vincenzo GENNARINO  
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I grew up in the beautiful city of Palermo, in southern Italy. I used to spend hours exploring the countryside and observing animal life. I was curious about everything then, and I still am.

During my doctoral studies at the TIGEM in Italy, in the lab of Sandro Banfi, my first publication was in the microRNA field. MicroRNAs (miRNAs) are small molecules that regulate the function of most human genes; the challenge has been to identify each miRNA's set of target genes. Various bioinformatic methods had been tried, but each approach reveals a different set of targets for a given microRNA. I took a different tack: I hypothesized that the target genes of a given miRNA are likely to belong to the same biological pathway and therefore to be co-expressed. This basic idea led me to develop HOCTAR (Genome Research, 2009) and then the more refined CoMeTa (Genome Research, 2012), whose prediction accuracy reaches nearly 100%, as calculated by analysis of previously characterized human miRNAs. CoMeTa was the first tool to infer the biological pathways of each human miRNA based on the identification of its set of target genes. HOCTAR led to the discovery of the function of miR-128, which controls the master gene TFEB (Science, 2009).

For my postdoctoral work I wanted to bring my background in bioinformatics and RNA biology to bear on problems in neuroscience, so I joined the lab of Huda Zoghbi. I studied the regulation of the epigenetic factor MECP2 during neurodevelopment (Genes & Development, 2013), the post-translational modification of a neurodegenerative disease protein, Ataxin1 (Cell, 2015 and Cell, 2018), and alternative polyadenylation (eLife, 2015). This work forms the basis of my lab's current projects.

#### Education & Training

MS, 2005 Biological Sciences, University of Palermo, Faculty of Medicine (Italy)  
hD, 2009 Medical Genetics, Second University of Naples (Italy)  
Fellowship: 2006 University of Milan (Italy)

#### Honors & Awards

- 2017 Young Investigator Research Grant 2018. "Delineating the PUM1 functional network in mice and humans." The National Ataxia Foundation.
- 2017 NARSAD Young Investigator Award 2018. "PUMILIO1 mutations cause two new neurological disorders: understanding its role in Mice and Humans." The Brain & Behavior Research Foundation.
- 2016 Young Investigator Research Grant 2017. "PUMILIO1 deficiency: understanding a new ataxia gene and its role in cerebellar dysfunction in mice and humans." The National Ataxia Foundation.
- 2016 Best Speaker Prize, 6th Ataxia Investigators Meeting (AIM), April 1, Orlando, Florida.
- 2016 Travel grant "Hot Chair" award as invited speaker to attend the 6th Ataxia Investigators Meeting (AIM), March 29-April 1, Orlando, Florida.

- 2016 First prize, “Best Paper” in the Department of Molecular and Human Genetics, Baylor College of Medicine Retreat, January 14-15, Galveston, TX.
- 2015 Winner, “Scientific Storytelling” Pediatric Research & Fellows’ Symposium, March 26, Department of Pediatrics, Texas Children’s Hospital, Houston, TX.
- 2012 Received National Scientific Qualification as Associate Professor in Experimental Biology, Ministry of Education, Universities and Research (MIUR).
- 2009 Young speaker special selection invitation to Keystone Symposia on Molecular and Cellular Biology – The Biology of RNA Silencing Meeting, April 25-30, Victoria British Columbia, Canada.
- 2007 One of 150 applicants selected to attend “Advanced Topics in Molecular Medicine,” July 15-18, at AREA Science Park (CBM-CEI) in Trieste, Italy.
- 2007 One of 100 applicants selected to attend the Accademia Nazionale dei Lincei Meeting, “The world of small non-coding RNAs,” June 11-12, Rome, Italy.
- 2006, 2007 Early Researcher Career Development Award provided by the Italian Ministry of Education, Universities and Research (MIUR) at the University of Milan.
- Research

My lab’s overall goal is to understand the molecular mechanisms driving neurological diseases, including isolated neuropsychiatric features, in the hope of ultimately devising viable therapies

Neuroscience made enormous strides during the 1990’s with the advent of molecular genetic techniques that allowed us to identify myriad disease genes and manipulate them in animal models from flies to mice. In the 2000’s, we came to appreciate the importance of epigenetic mechanisms to neurobiology, and now we are on the cusp of a new field that might be called “RNA neurobiology.”

RNA biology may, in fact, have particular importance in the brain, given the extremely dynamic nature of neuronal synapses. The post-synaptic compartment contains polysomes, which indicates that translation is crucial for higher-order brain activity, and protein synthesis has long been thought to be required for memory consolidation. Small wonder, then, that disruption of RNA-binding proteins is associated with wide-ranging syndromes that affect motor control, behavior, and cognition.

My interest in RNA-binding proteins centers on their role in post-transcriptional regulation of proteins that, when mutated, lead to human neurological disease. But my interest is in the wild-type versions of these proteins: my research has shown that relatively modest increases or decreases in the levels of at least some ‘normal’ proteins can be pathogenic. This opens up an entirely new avenue to discovering new neurological disease genes, as I showed recently in the identification of patients bearing mutations in Pumilio1 (Cell, 2018).

#### Research Interests

RNA-binding proteins and non-coding RNA regulatory networks in neurological disorders  
Establishment and maintenance of RNA homeostasis in the brain

Developing RNA therapeutic approaches to neurological diseases

Protein dosage and neurological disorders

## Grants

- National Ataxia Foundation Young Investigator Award (2017, 2018).
- NARSAD Young Investigator Award, Brain & Behavior Research Foundation (2018-2020).
- BRAIN & BEHAVIOR RESEARCH FOUNDATION NARSAD 2017 YOUNG INVESTIGATOR AWARD (Private)

Jan 15 2018 - Jan 14 2020

## Selected Publications

- Gennarino VA†, Palmer EE, McDonnell LM, Wang L, Adamski CJ, Koire A, See L, Chen CA, Schaaf CP, Rosenfeld JA, Panzer JA, Moog U, Hao S, Bye A, Kirk EP, Stankiewicz P, Breman AM, McBride A, Kandula T, Dubbs HA, Macintosh R, Cardamone M, Zhu Y, Ying K, Dias KR, Cho MT, Henderson LB, Baskin B, Morris P, Tao J, Cowley MJ, Dinger ME, Roscioli T, Caluseriu O, Suchowersky O, Sachdev RL, Lichtarge O, Tang J, Boycott KM, Holder JL, and Zoghbi HY†. “A mild PUM1 mutation is associated with adult-onset ataxia, whereas haploinsufficiency causes developmental delay and seizures.” *Cell*, 2018 Feb 22;172(5):924-936.e11. (†Corresponding authors).
- Gennarino VA\*, Alcott CA\*, Chen CA, Chaudhury A, Rosenfeld JA, Parikh S, Wheless JW, Roeder ER, Horovitz DDG, Roney EK, Smith JL, Cheung SW, Li W, Nailson JR, Schaaf CP, Zoghbi HY. “NUDT21-spanning CNVs lead to neuropsychiatric disease and altered MeCP2 abundance via alternative polyadenylation.” *eLife*, 2015 Aug 27;4. doi: 10.7554/eLife.10782. (\*Contributed equally).
- Gennarino VA, Singh RK, White JJ, De Maio A, Han K, Kim JY, Jafar-Nejad P, di Ronza A, Kang H, Sayegh LS, Cooper TA, Orr HT, Sillitoe RV and Zoghbi HY. “Pumilio1 Haploinsufficiency Leads to SCA1-like Neurodegeneration by Increasing Wild-Type Ataxin1 Levels.” *Cell*, 2015 Mar 12;160(6):1087-98. This paper was highlighted in an ALZ forum press release.
- Han K\*, Gennarino VA\*, Lee Y, Pang K, Hashimoto-Torii K, Choufani S, Raju CS, Oldham MC, Weksberg R, Rakic P, Liu Z, and Zoghbi HY. “Human-specific regulation of MeCP2 levels in fetal brains by microRNA miR-483-5p.” *Genes & Development*, 2013 Mar 1;27(5):485-90. (\*Contributed equally). This paper was selected for the journal cover.
- Gennarino VA, D’angelo G, Dharmalingam G, Fernandez S, Russolillo G, Sanges R, Mutarelli M, Belcastro V, Ballabio A, Verde P, Sardiello M, Banfi S. “Identification of microRNA-regulated gene networks by expression analysis of target genes.” *Genome Research*, 2012 Jun;22(6):1163-72. Epub 2012 Feb 24.
- Gennarino VA, Sardiello M, Avellino R, Meola N, Maselli V, Anand S, Cuttillo L, Ballabio A and Banfi S. “MicroRNA target prediction by expression analysis of host genes.” *Genome Research*, 2009 Mar;19(3):481-90. Epub 2008 Dec 16.