



Through Inspiration, Discovery
King Abdullah University of Science and Technology

Name: Valerio
Surname: Orlando
Nationality: Italian



Professor of Epigenetics
Director of KAUST Environmental Epigenetics Research
Program Biological and Environmental Sciences and
Engineering Division 4700 King Abdullah University of Science
and Technology Thuwal 23955-6900, Saudi Arabia
Email: Valerio.orlando@kaust.edu.sa
<https://keep.kaust.edu.sa>

Prof. Valerio Orlando obtained his PhD in Molecular Biology at University La Sapienza in Rome Italy, then he went on for postdoc in Epigenetics in Renato Paro's lab, at ZMBH Heidelberg (1991-1997) where he pioneered the worldwide used Chromatin Immunoprecipitation (ChIP) technology (Orlando and Paro, Cell 1993; Orlando et al EMBO J 1998, Orlando TIG 2000). In his subsequent work he carried on the work on the mechanistic role of Polycomb proteins cell memory system in the context of nuclear architecture, noncoding RNA and basal transcription regulation (Breiling et al, Nature 2001, Breiling et al, Mol Cell 2001, Orlando V Cell 2003, Lanzuolo et al Nat Cell Biol, 2007, Cernilogar et al Nature 2011).

He started his independent career in 1998 at San Raffaele Institute in Milan (Italy) where he established the Laboratory of Epigenetics and Genome reprogramming (first in Italy). In 2002 he joined Telethon Foundation and he moved to IGB CNR Campus in Naples (2002-2008) where he was founder member of the Dulbecco Telethon Institute (DTI), and later in Rome at Santa Lucia Foundation (2008-2013). He has been a proactive member of Eu-funded Network of Excellence of Epigenetics (Epigenome and Epigenesys Networks of Excellence) and together with Pino Macino he promoted the First National Italy's Flagship Project on Epigenetics (www.epigen.it). In 2013 He moved to KAUST where he founded the KAUST Environmental Epigenetics program (KEEP; keep.kaust.edu.sa).

Honors:

- Elected member of the European Molecular Biology Organization (EMBO) (2006)
- President of the Italian Society of Biophysics and Molecular Biology (SIBBM, www.sibbm.org) (2006-2012)

-Awarded “Cavaliere della Repubblica” (Knighthood) by the President of the Italian Republic (2007).

- RIKEN OMICs Center, FANTOM Consortium, Yokohama Japan (Senior Visiting Scientist)

Research Interests:

Prof. Orlando's interest is the exploration of the epigenetic mechanisms of adaptation and how these matter for development, ageing, nutrition and associated diseases. In particular, Prof. Orlando's lab investigates the chromatin and nuclear architecture mediated mechanisms that control and maintain cell identity and plasticity and in particular the contribution of the noncoding part of the genome and associated protein complex regulators. These include the “cell memory” chromosomal proteins called Polycomb and trithorax group and other chromatin structure regulators; (ii) the role of ncRNAs in epigenetic regulation and how this relates to development and adaptation, in particular in stress conditions (iii) the circadian clock and organ to organ communication. Furthermore, as part of the investigation of the plastic properties of the genome in response to developmental and environmental cues, Prof. Orlando's lab new focus has been exploring the functional role of the repetitive part of the mammalian genome (50% of total), in particular dynamics of mammalian transposable elements and their role in cell differentiation, reprogramming and disease. A major focus is Aging and RNA based potential therapeutic intervention for tissue homeostasis and regeneration in various aging related pathological contexts.

Selected Publications (last 5 years)

1. Bodega B, Marasca F, Ranzani V, Cherubini A, Della Valle F, Nguembor MV, Wassef M, Zippo A, Lanzuolo C, Pagani M, Orlando V. A cytosolic Ezh1 isoform modulates a PRC2---Ezh1 epigenetic adaptive response in postmitotic cells. *Nature Struct Mol Biol.* 2017 May;24(5):444
2. Li M, Borrelli E, Magistretti PJ, Izipisua Belmonte JC, Sassone---Corsi P, Orlando V. Gathering by the Red Sea highlights links between environment and epigenetics. *Nature Struct Mol Biol.* 2017 Jun 6;24(6):491-493
3. Marasca F, Bodega B, Orlando V. (2018). How Polycomb mediated cell memory deals with a changing environment. *Bioessays* Apr;40(4):e170013
4. Dyar KA, Lutter D, Artati A, Ceglia NJ, Liu Y, Armenta D, Jastroch M, Schneider S, de Mateo S, Cervantes M, Abbondante S, Tognini P, Orozco-Solis R, Kinouchi K, Wang C, Swerdloff R, Nadeef S, Masri S, Magistretti P, Orlando V, Borrelli E, Uhlenhaut NH, Baldi P, Adamski J, Tschöp MH, Eckel-Mahan K, Sassone-Corsi P. Atlas of Circadian Metabolism Reveals System-wide Coordination and Communication between Clocks. *Cell.* 2018 Sep 6;174(6):1571-1585
5. Shuaib M, Parsi KM, Thimma M, Adroub SA, Kawaji H, Seridi L, Ghosheh Y, Fort A, Fallatah B, Ravasi T, Carninci P, Orlando V. (2019) Nuclear AGO1 Regulates Gene Expression by Affecting Chromatin Architecture in Human Cells. *Cell Systems.* 9(5):446-45
6. Peng Liu, Muhammad Shuaib, Huoming Zhang, Seba S. Nadeef, Valerio Orlando. (2019) Ubiquitin ligases HUWE1 and NEDD4 cooperatively control signal dependent PRC2-Ezh1a/b mediated adaptive stress response pathway in skeletal muscle cells. *Epigenetics and Chromatin.* Dec 19;12(1):78.
7. Della Valle F, Thimma M, Caiazza M, Pulcrano, Celi, M, Adroub S, Liu P, Lobato G, Broccoli V, Orlando V. (2020). Transdifferentiation of Mouse Embryonic Fibroblasts into Dopaminergic Neurons reactivates LINE-1 repetitive elements. *Stem Cell Reports* (Jan 14;14(1):60-74
8. Bonetti A, et al, Gimenez J, et al...Orlando V* and Carninci P*, 2020 (RADICL-seq identifies general and cell type-specific principles of genome-wide RNA-chromatin interactions. *Nature Communications* Feb 24;11(1):1018 (* Co- corresponding authors)

9. Mangiavacchi A, Liu P, Della Valle F and Orlando V. (2021) New insights on the functional role of retrotransposons dynamics in mammalian somatic cells. ***Cell Mol Life Sci.*** 78(13):5245-5256.
10. El Said N, Della Valle F et al and Orlando V*(2021) Malat-1- PRC2-EZH1 interaction supports the oxidative stress dependent H3K27me3 remodeling in skeletal myotube. ***Cell Death and Disease*** 16;12(10):850.
11. Fallatah B, Shuaib M, Adroub S, Paytuv-Gallart A, Della Valle F, Nadeef S, Lanzuolo C, Orlando V. (2021). Ago1 controls myogenic differentiation by regulating eRNA mediated CBP guided epigenome reprogramming. ***Cell Reports*** 30;37(9):11006
12. Della Valle F, Reddy P.....Izpisua-Belmonte JC and Orlando V. (2022). L1-RNA is causative of heterochromatin erosion and target for amelioration of senescent phenotypes in progeroid syndromes. ***Science Translational Medicine (in press)***
13. *Mangiavacchi A,..... Izpisua Belmonte JC, Cinelli P, Gautvik KM, Orlando V. (2022). LINE 1 RNA delivery restores bone formation in osteoporotic human stem cells. (revised version at New England Journal of Medicine).*
14. Peng Liu, Seba Nadeef, et.... Paolo Sassone-Corsi & Valerio Orlando. Dual Role of PRC2-EZH1 in Orchestrating RNA Pol II Rhythmicity and epigenome structure in Circadian Transcription (***Nat Struct. Mol Biol, in revision***)