The Giovanni
Armenise-Harvard Foundation

Career Development Awardees

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Laurea	*University of Palermo (Italy), 1995*
Ph.D	*EMBL-University of Heidelberg (Germany) 2000*
Postdoc	*University College, Santa Cruz (USA) 2004*
Previous work experience	I became interested in chromatin dynamics during my graduate studies in Peter Becker's laboratory at EMBL-Heidelberg (Germany), where I characterized CHRAC, a *Drosophila* multi-subunit chromatin remodeling complex that uses the energy of ATP to mobilize nucleosomes and promote global chromatin fluidity. I found that ISWI, the catalytic subunit of CHRAC, is a nucleosome-stimulated ATPase. This molecular engine works together with other proteins in CHRAC to slide nucleosomes. These studies contributed to the molecular and biochemical characterization of CHRAC and revealed some of the mechanistic aspects of the chromatin remodeling reactions catalyzed by ATP-dependent chromatin remodeling complexes. To complement my extensive training in protein biochemistry, I obtained postdoctoral training in the use of classical and molecular genetics in John Tamkun's laboratory at UCSC. The aim of my postdoctoral work was to clarify the biological function of the ISWI ATPase by identifying factors with which it interacts *in vivo*. These studies showed that ISWI plays a global role in chromatin compaction and transcriptional repression. In particular I found that specific acetylation state of chromatin can influence the ability of ISWI to organize chromatin and regulate gene expression. These studies have shed light on the function and regulation of ISWI *in vivo* and improved our understanding of how the activity of ATP-dependent chromatin remodeling factors and histone modifying enzymes are coordinated.
Association memberships	

Research Interests

Eukaryotic cells store their genetic information in the form of chromatin, a complex of DNA packed with structural and regulatory proteins. The functional repeating unit of chromatin is the nucleosome, an octamer of histone proteins wrapped around 150 base pairs of DNA. Chromatin presents a barrier to many proteins that require access to DNA. Nuclear reactions therefore depend on molecular mechanisms that allow regulatory factors to gain access to DNA in chromatin. ATP-dependent chromatin remodeling and covalent modification of histone amino termini, including acetylation, methylation and phosphorylation, play central roles in determining chromatin accessibility.

Chromatin modifications, which occur without a change in DNA sequence, constitute the epigenetic markers of our genome. Epigenetic states of chromatin can influence a variety of nuclear processes that are dynamically carried out at the chromatin level. Specific combinations of epigenetic markers can establish a “histone code” that is interpreted by other regulatory proteins in the nucleus to direct downstream biological processes, including transcription, chromosome organization, DNA replication and repair. It is becoming clear that alterations in the spectrum of chromatin modifications underlie many human diseases. However, despite the wealth of data concerning the mechanisms of action of chromatin remodeling factors and histone modifying enzymes, relatively little is known about how their activities are coordinated to regulate chromatin structure, gene expression and other nuclear functions.

As an independent investigator I will use a combination of genetic and biochemical approaches to study how ATP-dependent chromatin remodeling activities are regulated and integrated into the larger regulatory network of post-translational modifications of chromatin. I am very confident that the combination of genetic and biochemical training that I obtained during the course of my scientific career will allow me to use ISWI and the fruit fly as a model system to understand chromatin dynamics at the molecular level.

Selected Publications

1) Galli-Stauber, C., Raho, G., Rossi, D., **Corona, D. F. V.**, Pirola, B., Bonaglia, M. C., Zuffardi, O., and Sorrentino, V. (1998). Genomic structure and chromosomal location of the human TGF -receptor interacting protein-1 (TRIP-1) gene to 1p34.1. **FEBS Lett** 426, 279-282.

2) Clapier, C. R., **Corona, D. F. V.**, Längst, G., Varga-Weisz, P. D., Becker, P. B (1998). CHRAC, a chromatin remodeling complex driven by the ATPase ISWI. “Transcriptional Regulation in Eukaryotes” Booklet, 65-71. **Ed. HFSP Press**

3) Corona, D. F. V., Längst, G., Clapier, C. R., Bonte, E. J., Ferrari, S., Tamkun, J. W., and Becker, P. B. (1999). ISWI is an ATP-dependent nucleosome remodeling factor. **Mol Cell** 3, 239-245.

4) Di Croce, L., Koop, R., Venditti, P., Westphal, H. M., Nightingale, K. P., **Corona, D. F. V.**, Becker, P. B., and Beato, M. (1999). Two-step synergism between the progesterone receptor and the DNA-binding domain of nuclear factor 1 on MMTV minichromosomes. **Mol Cell** 4, 45-54.

5) Längst, G., Bonte, E. J., **Corona, D. F. V.**, and Becker, P. B. (1999). Nucleosome movement by CHRAC and ISWI without disruption or trans-displacement of the histone octamer. **Cell** 97, 843-852.

6) Gebauer, F., **Corona, D. F. V.**, Preiss, T., Becker, P. B., and Hentze, M. W. (1999). Translational control of dosage compensation in *Drosophila* by Sex-lethal: cooperative silencing via the 5' and 3' UTRs of msl-2 mRNA is independent of the poly(A) tail. **EMBO J** 18, 6146-6154.

7) Corona, D. F. V., Eberharter, A., Budde, A., Deuring, R., Ferrari, S., Varga-Weisz, P., Wilm, M., Tamkun, J., and Becker, P. B. (2000). Two histone fold proteins, CHRAC-14 and CHRAC-16, are developmentally regulated subunits of chromatin accessibility complex (CHRAC). **EMBO J** 19, 3049-3059.

8) Poot, R. A., Dellaire, G., Hulsmann, B. B., Grimaldi, M. A., **Corona, D. F. V.**, Becker, P. B., Bickmore, W. A., and Varga-Weisz, P. D. (2000). HuCHRAC, a human ISWI chromatin remodelling complex contains hACF1 and two novel histone-fold proteins. **EMBO J** 19, 3377-3387.

9) Clapier, C. R., Längst, G., **Corona, D. F. V.**, Becker, P. B., and Nightingale, K. P. (2001). Critical role for the histone H4 N terminus in nucleosome remodeling by ISWI. **Mol Cell Biol** 21, 875-883.

10) Corona, D. F. V., Clapier, C. R., Becker, P. B., and Tamkun, J. W. (2002). Modulation of ISWI function by site-specific histone acetylation. **EMBO Rep** 3, 242-247.

11) Grüne, P. B., Brzeski, J., Eberharter, A., Clapier, C. R., **Corona, D. F. V.**, Becker, P. B., and Muller, C. W. (2003). Crystal structure and functional analysis of the nucleosome recognition module of the remodeling factor ISWI. **Mol Cell** 12, 449-460.

12) Corona, D. F. V., and Tamkun, J. W. (2004). Multiple Roles for ISWI in Transcription, Chromosome Organization and DNA Replication. **Biochim Biophys Acta.** 1677(1-3):113-9 (BBA Reviews Special Issue on: “Chromatin Structure and Function” Edited by Dr.Tony Imbalzano).

	13) Corona, D. F. V., Armstrong, J. A., and Tamkun, J. W. (2004). Genetic and Cytological Analysis of *Drosophila* Chromatin-remodeling Factors. **Methods in Enzymology** 377; 70-85 (Vol. A: "Chromatin and Chromatin Remodeling Enzymes", Edited by Dr.David Allis)
Laboratory Members	*Anna Sala, PostDoc* *Gaspare La Rocca, PostDoc* *Giosalba Burgio, PhD Student* *Walter Arancio, PhD Student* *Marianna Collesano, Technician* *Silvia Migliore, Technician*