BIOGRAPHICAL SKETCH

NAME: Dalla-Favera, Riccardo

eRA COMMONS USER NAME (credential, e.g., agency login): DALLAFAVERAR

POSITION TITLE: Professor of Clinical Medicine and Professor of Pathology and Cell Biology, Departments of Genetics and Development, Microbiology and Immunology, and Pathology and Cell Biology; Director, Institute for Cancer Genetics

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Milan, Milan, Italy	MD	05/1976	Medicine

A. Personal Statement

During the past 30 years, my research has focused on the molecular genetics of cancer, in particular on the pathogenesis of B cell malignancies, including Chronic Lymphocytic Leukemia, and Non-Hodgkin Lymphoma. My laboratory has identified a number of genetic lesions that contribute to the pathogenesis of these tumors, including the identification of the human c-MYC oncogene and its involvement in the chromosomal translocation associated with Burkitt Lymphoma, and the identification of the BCL6 oncogene, a major player in the pathogenesis of most human lymphomas. More recently, genomic analysis of Diffuse Large B cell Lymphoma (DLBCL), has led to the identification of additional genetic lesions that contribute to pathogenesis, including the inactivation of the chromatin modifier genes KTMDT2 and CREBBP/EP300, and loss of antigen-presenting molecules leading to immune escape. These results have been obtained using advanced genomic technologies, in vitro functional analysis of mutant genes, and validation in mouse models conditionally expressing the genetic lesions in B cells. These mouse models have been used to develop novel diagnostic and therapeutic approaches.

B. Positions and Honors

Positions and Employment

1983-1987 Assistant Professor, Department of Pathology, New York University School of Medicine, New York, NY
1987-1989 Associate Professor, Department of Pathology, New York University School of Medicine, New York, NY
1989-1991 Associate Professor, Department of Pathology, Columbia University, New York, NY
1991 - Professor, Department of Pathology, Columbia University, College of Physicians & Surgeons, New York, NY
1992-1998 Director, Division of Experimental Oncology, Department of Pathology, Columbia University, New York, NY
1992 - Professor, Department of Genetics & Development, Columbia University, New York, NY
1992 - Joanne and Percy Uris Professor of Clinical Medicine, Columbia University, New York, NY
1992-1997 Deputy Director, Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY
1999 - Director, Institute for Cancer Genetics, Columbia University, New York, NY
2005 - 2011 Director, Herbert Irving Comprehensive Cancer Center, New York, NY
2011 - Professor, Department of Microbiology and Immunology, Columbia University, New York, NY

Other Experience and Professional Memberships

1982 Member, American Association for the Advancement of Science
1983 Member, American Association for Microbiology

1984 Member, American Association of Pathologist
1988 Member, American Society of Hematology
1989-1994 Member, Pathology B Study Section, Division of Research Grants, NIH
1991 Member, American Association for Cancer Research
2000 - 2002 Co-Chair, Leukemia/Lymphoma/Myeloma Program Review Group, National Cancer Institute

Honors

1989 NIH, MERIT Award
1998 Fellow, American Association of Physicians
2002 NIH MERIT Award
2005 Outstanding Achievement Award, American-Italian Cancer Foundation
2005 William Dameshek Prize, American Society of Hematology
2010 Member, National Academy of Medicine, U.S.A.
2012 Alfred Knudson Award, National Cancer Institute
2014 Giants of Cancer Care Award
2015 Burkitt Medal Award, Trinity College, Dublin, Ireland
2015 Member, National Academy of Sciences, USA
2017 Fellow, American Association for Cancer Research Academy
2017 American Association for Cancer Research GHA Clowes Memorial Award
2017 The ARC Foundation Léopold Griffuel Award in Basic Research

C. Contribution to Science

1. ***Identification and Cloning of the c-MYC Proto-oncogene Locus and Demonstration of its Involvement in Gene Chromosomal Translocations in Burkitt Lymphoma:*** This work provided the first example (together with Ras gene mutations) of proto-oncogene alterations in human cancer, and the first evidence (together with BCR-ABL in CML) that cancer-associated chromosomal translocations directly involve proto-oncogene loci.
    a. **Dalla-Favera R,** Gelmann EP, Martinotti S, Franchini G, Papas TS, Gallo RC, and Wong-Staal F (1982). Cloning and characterization of different human sequences related to the onc-gene (v-myc) of avian myelocytomatosis virus (MC29). *Proc Nat Acad Sci USA,* 79(21), 6497-6501. PMCID: PMC347154
    b. **Dalla-Favera R**, Bregni M, Erikson J, Patterson D, Gallo RC, and Croce CM (1982). The human c-myc onc-gene is located on the region of chromosome 8 which is translocated in Burkitt lymphoma cells. *Proc Nat Acad Sci USA,* 79(24), 7824-7827. PMCID: PMC347441
    c. **Dalla-Favera R**, Martinotti S, Gallo RC, Erikson J, and Croce CM (1983). Translocation and rearrangements of the c-myc oncogene locus in human undifferentiated B-cell lymphomas. *Science,* 219(4587), 963-967. PMID: 6401867
    d. Gelmann EP, Psallidopoulos MC, Papas TS & Dalla-Favera R (1983). Identification of reciprocal translocation sites within the c-myc oncogene and immunoglobulin mu locus in a Burkitt lymphoma. Nature 306: 799-803.

2. ***Identification of the BCL6 Proto-oncogene as Part of the Common 3q27 Break in Diffuse Large B Cell Lymphoma (DLBCL), the Most Common B cell Lymphoma:*** Demonstration of the required role of BCL6 in the formation of germinal centers (GC) formation, the structure from which most B cell lymphomas derive. This work was followed by the demonstration of the role of BCL6 in controlling DNA repair via modulation of p53, and its role in inducing DLBCL in mouse models.
    a. Ye BH, Lista F, Lo Coco F, Knowles DM, Offit K, Chaganti RS, **Dalla-Favera R** (1993). Alterations of a zinc-finger encoding gene, BCL-6, in diffuse large-cell lymphoma. *Science,* 262(5134), 747-750. PMID: 8235596
    b. Ye BH, Cattoretti G, Zhang J, Hawe N, Shen Q, Orazi A, Nouri-Shirazi M, Chaganti RSK, Stall AM, Pandolfi PP, **Dalla-Favera R** (1997). The BCL-6 protooncogene controls germinal-centre formation and Th2-type inflammation. *Nat Genetics,* 16(2), 161-170. PMID: 9171827
    c. Phan R, **Dalla-Favera R** (2004). The BCL6 proto-oncogene suppresses p53 expression in germinal-center B cells. *Nature* 432(7017), 635-639. PMID: 15577913
    d. Cattoretti G, Pasqualucci L, Ballon G, Tam W, Nandula SV, Shen Q, Mo T, Murty VV, **Dalla-Favera R** (2005). Deregulated BCL6 expression recapitulates the pathogenesis of human diffuse large B-cell lymphomas in mice. Cancer Cell, 7(5), 445-455. PMID: 15894265

3. ***Evidence that the Somatic Hypermutation (SHM) Mechanism is Acting Outside the Immunoglobulin loci in Normal B cells and is Misfiring in DLBCL:*** this finding identifies a new mechanism of genetic lesion in DLBCL affecting coding and non-coding regulatory regions of numerous genes.
    a. Migliazza A, Martinotti S, Chen W, Fusco C, Ye B-H, Knowles DM, Offit K, Chaganti RSK, **Dalla-Favera R** (1995). Frequent somatic hypermutation of the 5' non-coding region of the BCL-6 gene in B cell lymphoma. *Proc Natl Acad Sci USA,* 92(26), 12520-12524. PMCID: PMC40389
    b. Pasqualucci L, Migliazza A, Fracchiolla N, William C, Neri A, Baldini L, Chaganti RSK, Klein U, Küppers R, Rajewsky K, **Dalla-Favera R** (1998). BCL-6 mutations in normal germinal center B cells: Evidence of somatic hypermutation acting outside Ig loci. *Proc Natl Acad Sci USA,* 95(20), 11816–11821. PMCID: PMC21723
    c. Pasqualucci L, Neumeister P, Goossens T, Gouri N, Chaganti RSK, Küppers R, **Dalla-Favera R** (2001). Hypermutation of multiple proto-oncogenes in B-cell diffuse large cell lymphoma. *Nature* 412(6844), 341-346. PMID: 11460166

4. ***Role of c-MYC in DNA Replication and in Germinal-Center Formation:*** these findings identify a novel non-transcriptional role of c-MYC and a new biological function of this gene in germinal-center formation with implications for normal biology and lymphomagenesis
    a. Dominguez-Sola D, Ying CY, Grandori C, Ruggiero L, Chen B, Galloway DA, Gu W, Gautier J, **Dalla-Favera R** (2007). Non-transcriptional control of DNA replication by c-myc. *Nature,* 448(7152), 445-451. PMID: 17597761
    b. Dominguez-Sola D, Victora GD, Ying CY, Phan RT, Saito M, Nussenzweig MC, **Dalla-Favera R** (2012). The proto-oncogene MYC is required for selection in the germinal center and cyclic reentry. *Nat Immunol*, 13(11),1083-1091. PMCID: PMC3711534

5. ***Srtuctural and Functional Genomics of DLBCL***
    a. Pasqualucci L, Dominguez-Sola D, Chiarenza A, Fabbri G, Grunn A, Trifonov V, Kasper LH, Lerach S, Ma J, Rossi D, Mullighan C, Rabadan R, Gaidano G, Brindle PK, **Dalla-Favera R** (2011). Inactivating mutations of acetyltransferase genes in B-cell lymphoma. *Nature*, 471(7337), 189-195, PMCID: PMC3271441
    b. Brescia, P., Schneider, C., Holmes, A.B., Shen, Q., Hussein, S., Pasqualucci, L., Basso, K., Dalla-Favera, R (2018) MEF2B Instructs Germinal Center Development and Acts as an Oncogene in B Cell Lymphomagenesis. Cancer Cell 10:34(3):453-465 PMID:30205047
    c. Scuoppo, C., Wang, J., Persaud, M., Mittan, S.K., Basso, K., Pasqualucci, L., Rabadan, R., Inghirami, G., Grandori, C., Bosch, F., **Dalla-Favera, R**. Repurposing Dasatinib for Diffuse Large B Cell Lymphoma. *Proc Natl Acad Sci USA* 116(34):16981-16986, 2019
    d. Holmes, A.B., Corinaldesi, C., Shen, Q., Kumar, R., Compagno, N., Wang, Z., Nitzan, M., Grunstein, E., Pasqualucci, L., **Dalla-Favera, R.**, Basso, K. Single-cell analysis of germinal-center B cells informs on lymphoma cell-of-origin and outcome. *J.Exp.Med*. (In Press)

Complete List of Published Work in MyBibliography:
http://icg.cpmc.columbia.edu/research-faculty/Riccardo-Dalla-Favera-publications