BIOGRAPHICAL SKETCH

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NAME: Montagna, Cristina

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POSITION TITLE: Professor of Radiation Oncology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Istituto Maria Ausiliatrice, Milano	BED	06/1986	Effective teaching methods
Istituto Gaetana Agnesi, Milano	N/A	06/1987	Idoneity to enter graduate program
University of Milano, Milano	PHD	07/1993	Cell and Molecular Biology
Consiglio Nazionale delle Ricerche (CNR), Milano	Postdoctoral Fellow	02/1999	Cancer Biology
National Institutes of Health (NIH), Bethesda, Maryland	Fellow	04/2004	Visiting fellow

A. Personal Statement

I am a cancer biologist with extensive expertise in molecular cytogenetic and cell biology. My laboratory has contributed significant work to the field of oncogene discovery, genomic instability in cancer, and age-related tissue degeneration. I trained with Prof. Renato Dulbecco (1975 Nobel Laureate for the discovery of SV40 DNA integration in oncogenically transformed cells) in oncogenes and tumor suppressor genes discovery using in culture systems of tumorigenesis. As a second postdoc, I was mentored by Dr. Thomas Ried, Chief of Cancer Genetics at NIH, who established Spectral Karyotyping (SKY), an advanced molecular cytogenetic technique based on Fluorescent in situ Hybridization (FISH) to simultaneously visualize all human or mouse chromosomes using pools of chromosome painting probes with unique chromatic properties. I applied SKY to measure aneuploidy and chromosome structural alterations to over 200 murine tumors from a variety of models for human cancer. As an independent investigator I continued functional work on oncogene discovery, especially in breast and cervical carcinogenesis. More recently I studied the functional consequences of genomic instability, particularly aneuploidy, on cell fitness to reveal molecular mechanisms that underlie age related increased risk to develop cancer. This new line of work offered me opportunities to apply second and third generation sequencing and master single cell genomic methodologies. My laboratory was the first to report age related accumulation of aneuploidy and was the first to inform that aneuploidy in the absence of tolerating mutations induce cellular senescence with the activation of a senescence-associated secretory phenotype (SASP). Throughout my training and my independent career, I gained expertise in molecular and cellular biology, cancer genetics, FISH techniques, and single cell genomics. My laboratory leads research projects with a focus on genomic instability and functional outcomes with a particular emphasis on risk factors and modulators of tumor initiation, both within the Rutgers Cancer Center and through multi-institutional projects. My expertise complements Dr. Chang's background in computational biology and through our joint efforts we are well positioned to be Program Co-Leaders of the Genomic Instability and Cancer Genetics Research Program on the Cancer Center Support Grant.

Citations:

1. Sun S, Brazhnik K, Lee M, Maslov AY, Zhang Y, Huang Z, Klugman S, Park BH, Vijg J, **Montagna C**. Single-cell analysis of somatic mutation burden in mammary epithelial cells of pathogenic BRCA1/2 mutation carriers. J Clin Invest. 2022 Mar 1;132(5) PubMed Central PMCID: PMC8884908.
2. Van Arsdale A, Patterson NE, Maggi EC, Agoni L, Van Doorslaer K, Harmon B, Nevadunsky N, Kuo DYS, Einstein MH, Lenz J, Montagna C. Insertional oncogenesis by HPV70 revealed by multiple genomic

analyses in a clinically HPV-negative cervical cancer. Genes Chromosomes Cancer. 2020 Feb;59(2):84-95. PubMed Central PMCID: PMC6916423.

3. Andriani GA, Almeida VP, Faggioli F, Mauro M, Tsai WL, Santambrogio L, Maslov A, Gadina M, Campisi J, Vijg J, **Montagna C**. Whole Chromosome Instability induces senescence and promotes SASP. Sci Rep. 2016 Oct 12;6:35218. PubMed Central PMCID: PMC5059742.
4. Andriani GA, Faggioli F, Baker D, Dollé ME, Sellers RS, Hébert JM, Van Steeg H, Hoeijmakers J, Vijg J, **Montagna C**. Whole chromosome aneuploidy in the brain of Bub1bH/H and Ercc1-/Δ7 mice. Hum Mol Genet. 2016 Feb 15;25(4):755-65. PubMed Central PMCID: PMC4743693.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2022 -	Co-leader Genomic Instability and Cancer Genetics Research Program, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2021 -	Professor of Radiation Oncology, RBHS -CANCER INSTITUTE OF NEW JERSEY
2021 -	Adjunct Professor of Genetics and Pathology, ALBERT EINSTEIN COLLEGE OF MEDICINE, INC, New York, NY
2020 - 2021	Professor of Genetics, ALBERT EINSTEIN COLLEGE OF MEDICINE, INC
2013 - 2020	Associate Professor Of Genetics and Pathology, ALBERT EINSTEIN COLLEGE OF MEDICINE, INC, New York, NY
2004 - 2013	Assistant Professor of Genetics and Pathology, Albert Einstein College of Medicine, New York, NY

Honors

2003 - 2003	Center for Cancer Research exceptional pay increase award for outstanding researcher, NIH
2001 - 2001	Abstract winner of NIH travel FARE, NIH

C. Contribution to Science

1. Discovery of that somatic low-level aneuploidy is present in disease free tissues, and that chromosome specific aneuploidies accumulated during normative aging. During my postdoctoral training I applied Fluorescent in situ Hybridization (FISH) to the analysis of a large number of tumors form a variety of murine models of human cancer. Transitioning into my independent career I became interested in exploring the possibility that stochastic numerical chromosome changes occur at sub clonal levels in disease free tissues and like other forms of genomic instability accumulate with age contributing to age related tissue dysfunction. My laboratory performed extensive and detailed analysis of aneuploidy in different human tissues and murine models. We demonstrated, for the first time, that whole-chromosome aneuploidies accumulate during aging with potential deleterious functional impact and proposed to be more common than anticipated.

    a. Andriani GA, Faggioli F, Baker D, Dollé ME, Sellers RS, Hébert JM, Van Steeg H, Hoeijmakers J, Vijg J, **Montagna C**. Whole chromosome aneuploidy in the brain of Bub1bH/H and Ercc1-/Δ7 mice. Hum Mol Genet. 2016 Feb 15;25(4):755-65. PubMed Central PMCID: PMC4743693.
    b. Faggioli F, Wang T, Vijg J, **Montagna C**. Chromosome-specific accumulation of aneuploidy in the aging mouse brain. Hum Mol Genet. 2012 Dec 15;21(24):5246-53. PubMed Central PMCID: PMC3510757.
    c. Faggioli F, Vezzoni P, **Montagna C**. Single-cell analysis of ploidy and centrosomes underscores the peculiarity of normal hepatocytes. PLoS One. 2011;6(10):e26080. PubMed Central PMCID: PMC3192148.
    d. Faggioli F, Sacco MG, Susani L, **Montagna C**, Vezzoni P. Cell fusion is a physiological process in mouse liver. Hepatology. 2008 Nov;48(5):1655-64. PubMed PMID: 18925640.

2. Contributions to the field of genomic instability and its functional outcomes. Building on our seminal discoveries that aneuploidy is found in non-cancer tissues we developed the hypothesis that aneuploidy may be a form of genomic instability contributing to tissue degeneration and organ dysfunction at old age. To test this hypothesis, we set up both in culture and in vivo systems. Our publication in 2016 demonstrated that aneuploidy is sufficient to promote premature senescence in primary fibroblasts. Aneuploidy induced

senescent cells were strikingly similar to senescent cells induced by continuous replication but occurred in a much shorter period of time. We first reported that aneuploid cells secrete chemokines and cytokines producing a senescence-associated secretory phenotype (SASP) similar but unique to that of replicative senescence and senescent cells induced by other stressors. In addition to my own work, I collaborated with experts in the field of aneuploidy. In addition to our own studies, we provided our expertise to support studies in genomic instability to other groups.

a. Dong X, Sun S, Zhang L, Kim S, Tu Z, **Montagna C**, Maslov AY, Suh Y, Wang T, Campisi J, Vijg J. Age-related telomere attrition causes aberrant gene expression in sub-telomeric regions. Aging Cell. 2021 Jun;20(6):e13357. PubMed Central PMCID: PMC8208793.
b. Patkar S, Heselmeyer-Haddad K, Auslander N, Hirsch D, Camps J, Bronder D, Brown M, Chen WD, Lokanga R, Wangsa D, Wangsa D, Hu Y, Lischka A, Braun R, Emons G, Ghadimi BM, Gaedcke J, Grade M, **Montagna C**, Lazebnik Y, Difilippantonio MJ, Habermann JK, Auer G, Ruppin E, Ried T. Hard wiring of normal tissue-specific chromosome-wide gene expression levels is an additional factor driving cancer type-specific aneuploidies. Genome Med. 2021 May 25;13(1):93. PubMed Central PMCID: PMC8147418.
c. Andriani GA, Almeida VP, Faggioli F, Mauro M, Tsai WL, Santambrogio L, Maslov A, Gadina M, Campisi J, Vijg J, **Montagna C**. Whole Chromosome Instability induces senescence and promotes SASP. Sci Rep. 2016 Oct 12;6:35218. PubMed Central PMCID: PMC5059742.
d. Weaver BA, Silk AD, **Montagna C**, Verdier-Pinard P, Cleveland DW. Aneuploidy acts both oncogenically and as a tumor suppressor. Cancer Cell. 2007 Jan;11(1):25-36. PubMed PMID: 17189716.

3. Development of tools to study aneuploidy. Most of the methods commonly used to study aneuploidy have been developed for the analysis of the cancer genome where clonal cells, often with high DNA copy number variation, are present. Other methods have been refined to detected germline copy number changes (i.e., prenatal diagnosis or detection of CNVs in congenital disorders). The study of aneuploidy in somatic disease-free tissues is challenged by unique features: the random distribution of Copy Number Alterations (CNAs), or segmental CNAs, that result from Chromosome Instability (CIN) before the acquisition of clonal populations and the low frequency of affected cells (often in the range of 1-10% of the total population). We developed customized methodologies and analytical tools to overcome some of these challenges.

a. Andriani GA, Maggi E, Piqué D, Zimmerman SE, Lee M, Quispe-Tintaya W, Maslov A, Campisi J, Vijg J, Mar JC, **Montagna C**. A direct comparison of interphase FISH versus low-coverage single cell sequencing to detect aneuploidy reveals respective strengths and weaknesses. Sci Rep. 2019 Jul 19;9(1):10508. PubMed Central PMCID: PMC6642082.
b. Piqué DG, Andriani GA, Maggi E, Zimmerman SE, Greally JM, **Montagna C**, Mar JC. Aneuvis: web-based exploration of numerical chromosomal variation in single cells. BMC Bioinformatics. 2019 Jun 17;20(1):336. PubMed Central PMCID: PMC6580570.
c. Maggi EC, Gravina S, Cheng H, Piperdi B, Yuan Z, Dong X, Libutti SK, Vijg J, Montagna C. Development of a Method to Implement Whole-Genome Bisulfite Sequencing of cfDNA from Cancer Patients and a Mouse Tumor Model. Front Genet. 2018;9:6. PubMed Central PMCID: PMC5787102.
d. Faggioli F, Vijg J, **Montagna C**. Four-color FISH for the detection of low-level aneuploidy in interphase cells. Methods Mol Biol. 2014;1136:291-305. PubMed PMID: 24633803.

4. Discovery of novel oncogenes and tumor suppressor genes and role of genomic instability in carcinogenesis. During my first PhD training I worked at the National Research Council in Milano, Italy, under the supervision of Prof. Renato Dulbecco on a project aimed to identify new genes of breast tumor initiation. My investigation resulted in the identification of novel genes important for mammary gland differentiation, the roles of which have been subsequently characterized by us and others in human tumorigenesis. As an independent investigator I continued to study mammary gland development and published the first complete gene expression dataset of luminal and basal mammary epithelial cells across all stages of pregnancy, lactation and involution which identified new regulatory pathways. More recently, I studied the role of genomic instability in breast cancer initiation.

a. Sun S, Brazhnik K, Lee M, Maslov AY, Zhang Y, Huang Z, Klugman S, Park BH, Vijg J, **Montagna C**. Single-cell analysis of somatic mutation burden in mammary epithelial cells of pathogenic BRCA1/2 mutation carriers. J Clin Invest. 2022 Mar 1;132(5) PubMed Central PMCID: PMC8884908.
b. Van Arsdale A, Patterson NE, Maggi EC, Agoni L, Van Doorslaer K, Harmon B, Nevadunsky N, Kuo DYS, Einstein MH, Lenz J, **Montagna C**. Insertional oncogenesis by HPV70 revealed by multiple genomic analyses in a clinically HPV-negative cervical cancer. Genes Chromosomes Cancer. 2020 Feb;59(2):84-95. PubMed Central PMCID: PMC6916423.
c. Acosta D, Bagchi S, Broin PÓ, Hollern D, Racedo SE, Morrow B, Sellers RS, Greally JM, Golden A, Andrechek E, Wood T, **Montagna C**. LPA receptor activity is basal specific and coincident with early pregnancy and involution during mammary gland postnatal development. Sci Rep. 2016 Nov 3;6:35810. PubMed Central PMCID: PMC5093903.
d. Acosta D, Suzuki M, Connolly D, Thompson RF, Fazzari MJ, Greally JM, **Montagna C**. DNA methylation changes in murine breast adenocarcinomas allow the identification of candidate genes for human breast carcinogenesis. Mamm Genome. 2011 Apr;22(3-4):249-59. PubMed PMID: 21373886.

5. Discovery and functional characterization of the novel oncogene Septin 9. While at NIH I identified Septin 9 (SEPT9), a GTP-binding protein interacting with the cytoskeleton, as amplified in the form of double minutes chromosomes in mouse mammary tumors and proposed SEPT9 as a novel oncogene. Up to my findings SEPT9 was assumed to act as a tumor suppressor gene because of its previous mapping to regions of LOH in human breast cancer patients. My original publication proposing SEPT9 as a novel oncogene is highly cited. In my own laboratory I continue the work on SEPT9 with the ultimate goal to elucidate the functional consequences of SEPT9 amplification and over expression in breast cancer. Of note, SEPT9 became an important biomarker in the screening for colorectal cancer, it was the first is cell free DNA screen FDA approved for colorectal cancer detection.

    a. Marcus J, Bejerano-Sagie M, Patterson N, Bagchi S, Verkhusha VV, Connolly D, Goldberg GL, Golden A, Sharma VP, Condeelis J, **Montagna C**. Septin 9 isoforms promote tumorigenesis in mammary epithelial cells by increasing migration and ECM degradation through metalloproteinase secretion at focal adhesions. Oncogene. 2019 Jul;38(30):5839-5859. PubMed Central PMCID: PMC6859949.
    b. Connolly D, Hoang HG, Adler E, Tazearslan C, Simmons N, Bernard VV, Castaldi M, Oktay MH, **Montagna C**. Septin 9 amplification and isoform-specific expression in peritumoral and tumor breast tissue. Biol Chem. 2014 Feb;395(2):157-67. PubMed PMID: 24127542.
    c. Connolly D, Yang Z, Castaldi M, Simmons N, Oktay MH, Coniglio S, Fazzari MJ, Verdier-Pinard P, **Montagna C**. Septin 9 isoform expression, localization and epigenetic changes during human and mouse breast cancer progression. Breast Cancer Res. 2011 Aug 10;13(4):R76. PubMed Central PMCID: PMC3236340.
    d. **Montagna C**, Lyu MS, Hunter K, Lukes L, Lowther W, Reppert T, Hissong B, Weaver Z, Ried T. The Septin 9 (MSF) gene is amplified and overexpressed in mouse mammary gland adenocarcinomas and human breast cancer cell lines. Cancer Res. 2003 May 1;63(9):2179-87. PubMed PMID: 12727837.

Complete List of Published Work in My Bibliography:
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