BIOGRAPHICAL SKETCH

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NAME: Sidoli, Simone

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

POSITION TITLE: Assistant Professor, Department of Biochemistry

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)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Parma, Italy	B.S.	09/2007	Biotechnology
University of Parma, Italy	M.S.	02/2010	Industrial Biotechnology
University of Southern Denmark, Odense, Denmark	Ph.D.	12/2013	Biochemistry
University of Southern Denmark, Odense, Denmark	Res. Fellow	03/2014	Biochemistry
University of Pennsylvania, Philadelphia, PA, USA	Postdoc	02/2019	Biochemistry

A. Personal Statement

Our group develops and utilizes biochemical methods to identify the state and the dynamics of chromatin in health and disease. Specifically, we focus on identifying **the proteins and cell phenomena that maintain chromatin homeostasis**. Anomalous changes in the equilibrium that maintains proper chromatin compaction and dynamics is associated with the development of diseases such as cancer, diabetes, and the reversing of latency of DNA-integrated viruses. In addition, chromatin decondenses during healthy aging, making the consequences of this phenomenon universal for all living organisms. I have optimized different workflows to study protein modifications, in particular proteins associated with the backbone of chromatin, i.e. histones. My methods have shed light on the cross-talk between histone modifications and predict the function of some uncharacterized histone codes. I spent my postdoc focusing on applying mass spectrometry to investigate the chromatin compaction state and dynamics of systems undergoing metabolic changes.

As proteomics lab, we are also heavily invested in developing methods to study protein-protein interactions, protein post-translational modifications, and protein translational rate. We have applied our methods to approx. 150 different projects per year since the inception of our Core in 2019, publishing nearly 60 peer-reviewed articles in collaboration with other laboratories.

Now, I have created and I intend to keep pursuing a **highly diverse lab**, where trainees of all levels are equal. Our lab has created a synergy within the team, where the research team seamlessly integrates projects with the more experienced personnel of the proteomics core, and vice versa. As well, I have four members shared in between our lab a close collaborator (2 students and 2 postdocs), which have provided a tremendous source of new ideas and complementary approaches. Our lab has grown **a large interdisciplinary network** in less than 3 years. We are members of the Einstein Cancer Center, the Nathan Shock Center for excellence on Biology of Aging Research (E-NSC), the ERC-CFAR Einstein-Rockefeller-CUNY Center for AIDS research and the Einstein Institute for Neuroimmunology and Inflammation. Our technology is very versatile, and I consider it perfectly suitable for the project described in this application as well. I have a long-term experience with combining chromatin modification data with cell phenotype, as discussed in sections 1, 3 and 4 of “Contribution to Science”.

Aging funding (and critical instrument support) that I would like to highlight include:

1S10OD030286-01 (PI: Sidoli) 05/15/2021 – 05/14/2022 In-kind
NIH, Office of the Director $600,000
Role: PI/PD
Title: Orbitrap Exploris 480 Basic System

Sagol Network GerOmic Award (PI: Sidoli) 12/31/2020 – 12/31/2022 2.4 calendar
American Federation for Aging Research (AFAR) $100,000
Role: PI
Title: Accessible heterochromatin in exceptional longevity, a proteomics signature

Merck/MSD (PI: Sidoli) 08/09/2021 – 12/08/2022 In-kind
Merck/MSD $50,000 (1 year)
Role: PI
Title: High-Throughput Peptide Mapping for ADC Reaction Monitoring

NAM Healthy Longevity (PI: Sidoli, Arioka, Basu) 05/25/2020 – 03/31/2021 In-kind
Japan Agency for Medical Research and Development $23,500 (1 year)
Role: co-PI
Title: Histone modifications as new targets for pathophysiology of accelerated brain aging associated with mental disorders: Application for development of treatment and diagnostic method

Interstellar initiative (PI: Sidoli, Arioka, Basu) 9/14/2019 – 2/21/2020 In-kind
NYAS and the Japan Agency AMED $27,000
Role: co-PI
Title: Schizophrenia in aging towards next-generation therapy

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2020-	Scientific Director of the Proteomics Core, Albert Einstein College of Medicine, NY, USA
2019-	Tenure-Track Assistant Professor, Albert Einstein College of Medicine, NY, USA
2017	Guest scientist, The Children's Hospital of Philadelphia, PA, USA
2014-2019	Postdoctoral fellow, University of Pennsylvania, PA, USA
2013-2014	Research fellow, University of Southern Denmark
2010-2013	Ph.D. fellow in Biochemistry and Molecular Biology, University of Southern Denmark
2010	Research assistant, University of Parma, Italy

Awards and Honors

2022	Eastern Analytical Symposium Young Investigator Award
2020-2021	SARS-CoV-2 (COVID-19) Research Microgrant sponsored by Einstein-Montefiore
2020-2021	NAM Healthy Longevity Grand Challenge Catalyst award
2019	Nominated in the Top10 Italian scientists under 40 by the magazine Fortune Italia
2019	Umberto Mortari Award sponsored by Merck/MSD Italia, Rome, Italy
2018	BPP Award from the University of Pennsylvania, PA, USA

Scientific appointments

2021-2023	Fonds Wetenschappelijk Onderzoek (FWO) College Panel reviewer (Brussels, Belgium)
2021-	Member of the Einstein Institute for Neuroimmunology and Inflammation
2020-	Scientific partner with Medivac Srl, Parma, Italy
2020-	Member of the ERC-CFAR Einstein-Rockefeller-CUNY Center for AIDS research
2020-	Member of the Nathan Shock Center for excellence on Biology of Aging Research
2019-	Center of Excellence for CelVivo, Odense, Denmark
2019-	Member of the Einstein Cancer Center
2018-	Scientific advisor of Immagina BioTechnology, Trento, Italy

C. Contribution to Science

1. Identification of chromatin dynamics in model systems

The methods I developed utilizing mainly mass spectrometry have been used to investigate epigenetic features of different model systems. Pulsed metabolic labeling combined with histone peptide analysis was used to identify in a large-scale manner which histone modifications are in highly transcribed chromatin loci (ref. i). Metabolic labeling was also used to discriminate old from newly synthesized histone proteins; this was applied to determine how histone marks are recycled during the cell cycle and thus how epigenetic traits are inherited (ref. ii). We exploited middle-down proteomics to predict the function of uncharacterized histone post-translational modifications; for instance, we identified the histone mark H3K23me2, non-existing in mammals, as critical player in forming compact chromatin in *C. elegans* (ref. iii). I then utilized physical chromatin separation to identify the proteome occupying compacted vs accessible chromatin (ref. iv).

i. A mass spectrometry-based assay using metabolic labeling to rapidly monitor chromatin accessibility of modified histone proteins
***Sidoli S**, Lopes M, Lund PJ, Goldman N, Fasolino M, Coradin M, Bhanu NV, Kulej K, Vahedi G and Garcia BA (Scientific Reports, 2019)*

ii. Two distinct modes for propagation of histone PTMs across the cell cycle
*Alabert C, Barth TK, Reverón-Gómez N, **Sidoli S**, Schmidt A, Jensen ON, Imhof A and Groth A (Genes and Development, 2015)*

iii. H3K23me2 is a New Heterochromatic Mark in Caenorhabditis elegans
*Vandamme J, **Sidoli S**, Mariani L, Friis C, Jensen ON and Salcini AE (Nucleic Acid Research, 2015)*

iv. Genomic and Proteomic Resolution of Heterochromatin and Its Restriction of Alternate Fate Genes
*Becker JS, McCarthy RL, **Sidoli S**, Donahue G, Kaeding KE, He Z, Lin S, Garcia BA and Zaret KS (Molecular Cell, 2017)*

2. Development of methods for chromatin analysis based on mass spectrometry (MS)

The early focus of my research has been advancing the detection and identifying different properties of chromatin modifications. I have optimized the proteomics approach to quantify single and binary histone post-translational modifications (ref. i). This acquisition method is currently the most used in scientific publications investigating histone marks via MS. Next, I actively contributed to the optimization of the “middle-down” MS strategy, allowing for the characterization of intact N-terminal tails, which can be used to identify histone combinatorial codes. After optimizing the workflow (ref. ii), I demonstrated that histone sequences and modifications can be pulse-labeled to study their turnover and the order of their deposition (ref. iii). More recently, I developed an ultra-throughput direct injection system to analyze histone modifications via MS in less than one minute and with enhanced reproducibility (ref. iv).

i. Low resolution data-independent acquisition in an LTQ-Orbitrap allows for simplified and fully untargeted analysis of histone samples
***Sidoli S**, Simithy-Williams J, Karch KR, Kulej K and Garcia BA (Analytical Chemistry, 2015)*

ii. Middle-down hybrid chromatography/tandem mass spectrometry workflow for characterization of combinatorial post-translational modifications in histones
***Sidoli S**, Schwämmle V, Ruminowicz C, Hansen TA, Wu X, Helin K and Jensen ON (Proteomics, 2014)*

iii. Metabolic labeling in middle-down proteomics allows for investigation of the dynamics of the histone code
***Sidoli S**, Lu C, Coradin M, Wang X, Karch KR, Ruminowicz C and Garcia BA (Epigenetics & Chromatin, 2017)*

iv. One minute analysis of histone post-translational modifications by direct injection mass spectrometry
***Sidoli S**, Kori Y, Lopes M, Yuan ZF, Kim HJ, Kulej K, Janssen K, Agosto L, Cunha JPC and Garcia BA (Genome Research, 2019)*

3. Cross-talk between chromatin modifications and metabolism

A major goal of my research is understanding the cross-talk between chromatin modifications and metabolism. In the past year, I have applied methods to identify how methionine starvation affects compact heterochromatin and spurious transcription (ref. i, senior author). Next, I investigated how glucose starvation induces cells to recycle acetylation from reservoir protein residues to sites for activating gene expression (ref. ii). Finally, I investigated how nuclear availability of acyl-CoA affects the levels of histone modifications (ref. iii).

i. A Key Silencing Histone Mark on Chromatin Is Lost When Colorectal Adenocarcinoma Cells Are Depleted of Methionine by Methionine γ-Lyase
Raboni S, Montalbano S, Stransky S, Garcia BA, Buschini A, Bettati S, ***Sidoli S*** *and Mozzarelli A (Frontiers in Molecular Biosciences, 2021)*

ii. Enzymatic transfer of acetate on histones from lysine reservoir sites to lysine activating sites
Mendoza M, Egervari G, ***Sidoli S****, Donahue G, Alexander DC, Sen P, Garcia BA and Berger SL (Science Advances, 2022)*

iii. Quantitative subcellular acyl-CoA analysis reveals distinct nuclear metabolism and isoleucine-dependent histone propionylation
Trefely S, Huber K, Liu J, Noji M, Stransky S, Singh J, Doan MT, Lovell CD, von Krusenstiern E, Jiang H, Bostwick A, Pepper HL, Izzo L, Zhao S, Xu JP, Bedi KC Jr, Rame JE, Bogner-Strauss JG, Mesaros C, ***Sidoli S****, Wellen KE and Snyder NW (Molecular Cell, 2022)*

4. Application of in-house developed methods to understand cell development and disease etiology

The methods I established have been exploited to define different aspects of phenotype dynamics in cells. We have discovered that metabolic imbalance can alter the levels of histone acetylation and augment the level of other acyl marks derived from the beta-oxidation of fatty acids (ref. i). I have contributed to characterize how markers of constitute heterochromatin are differentially deposited during hepatic and pancreatic cell differentiation (ref. ii). Altered levels of histone acetylation were also linked to pancreatic tumorigenesis (ref. iii). Finally, using metabolic labeling we have linked alcohol intake to changes in brain histone acetylation (ref. iv).

i. Characterization of histone acylations links chromatin modifications with metabolism
Simithy J, ***Sidoli S****, Yuan ZF, Coradin M, Bhanu NV, Marchione DM, Klein BJ, Bazilevsky GA, McCullough CE, Magin RS, Kutateladze TG, Snyder NW, Marmorstein R and Garcia BA (Nature Communications, 2017)*

ii. H3K9me3-heterochromatin loss at protein-coding genes enables developmental lineage specification
Nicetto D, Donahue G, Jain T, Peng T, ***Sidoli S****, Sheng L, Montavon T, Becker JS, Grindheim JM, Blahnik K, Garcia BA, Tan K, Bonasio R, Jenuwein T and Zaret KS (Science, 2019)*

iii. Acetyl-CoA Metabolism Supports Multistep Pancreatic Tumorigenesis
Carrer A, Trefely S, Zhao S, Campbell SL, Norgard RJ, Schultz KC, ***Sidoli S****, Parris JLD, Affronti HC, Sivanand S, Egolf S, Sela Y, Trizzino M, Gardini A, Garcia BA, Snyder NW, Stanger BZ and Wellen KE (Cancer Discovery, 2019)*

iv. Alcohol metabolism contributes to brain histone acetylation
Mews P, Egervari G, Nativio R, ***Sidoli S****, Donahue G, Lombroso SI, Alexander DC, Riesche SL, Heller EA, Nestler EJ, Garcia BA and Berger SL (Nature, 2019)*

5. Reviews, protocol papers, book chapters and commentaries

Finally, I have contributed to numerous reviews, protocol papers and commentaries. These manuscripts include reviews about state-of-the-art proteomics data analysis (ref. i), protocols I personally contributed to optimize (ref. ii) and reviews about state-of-the-art chromatin analysis (ref. iii). Moreover, I contributed to reviewing more niche applications like middle-down MS (ref. iv).

i. Guide for protein fold change and p-value calculation for non-experts in proteomics
Aguilan J, Kulej K and ***Sidoli S*** *(Molecular Omics, 2020)*

ii. Characterization of individual histone post-translational modifications and their combinatorial patterns by mass spectrometry-based proteomics strategies
Sidoli S *and Garcia BA (Methods in Molecular Biology, book chapter, 2016)*

iii. Mass spectrometry to study chromatin compaction
Stransky S, Aguilan J, Lachowicz J, Madrid-Aliste C, Nieves E and ***Sidoli S*** *(Biology, 2020)*

iv. Middle-down proteomics: a still unexploited resource for chromatin biology
Sidoli S *and Garcia BA (Expert Review of Proteomics, 2017)*

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1VMclAulxGy5j/bibliography/public/
Total peer-reviewed publications: 169; First-author publications: 22; Corresponding author publications: 13