BIOGRAPHICAL SKETCH

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NAME: De Carvalho Daniel D

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

POSITION TITLE: Full Professor

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 Brasilia, Brazil	B.Sc.	12/2005	Veterinary Sciences
University of São Paulo, Brazil	Ph.D	12/2009	Immunology and Molecular Biology
University of Southern California	Post-Doc	06/2012	Cancer Epigenetics and Bioinformatics

A. Personal Statement

I am Full Professor in the Department of Medical Biophysics, University of Toronto, Senior Scientist at Princess Margaret Cancer Centre, University Health Network. Moreover, in recognition of my previous achievements, I hold the Helen M Cooke endowed professorship in Cancer Epigenetics and I am the Canada Research Chair in Cancer Epigenetics and Epigenetic therapy. My research program focuses on translational aspects of cancer epigenetics, with especial emphasis on DNA methylation. My group is interested epigenetic regulation of transposable elements (TEs) and the effects TEs dysregulation in cancer development and cancer therapy. We first described the 'viral mimicry' response, when cancer cells reactivate TEs, leading to an innate anti-viral response, loss of cancer cell fitness, adaptive immune response and increase sensitivity to immune checkpoint therapies (Roulois, Cell 2015; Sheng, Cell 2018; Ishak, Trends in Cancer 2018; Krug, Cancer Cell 2019; Mehdipour, Nature 2020; Deblois, Cancer Discovery 2020; Chen, Cancer Discovery 2021; and Šulc, BioRxiv 2021).

Moreover, my group is interested in understanding the role of epigenetic regulation in immune cells and how to take advantage of this for cancer therapy (Benevides, Cancer Research 2015; Shinde, Nature Immunology 2018; Chakravarthy, Nature Communications 2018; Jones, Nature Reviews Cancer 2019; Yau, Trends in Cell Biology 2018; Halaby, Science Immunology 2019; Taylor, JITC 2020; Yau, Molecular Cell 2021; Yau, Star Protocols 2021).

Finally, my group have pioneered the use of DNA methylation as biomarker for cancer early detection, subgroup classification and monitoring therapy response using both tissue or plasma/urine derived cfDNA (Torchia, Cancer Cell 2016; Burgener, Seminars in Oncology 2017; Shen, Nature 2018; Shen, Nature Protocols, 2019; Nassiri, Nature Medicine 2020; Nuzzo, Nature Medicine 2020; Chen, Nature Cell Biology 2021; Zuccato, Neuro-Oncology 2021; Burgener, Clinical Cancer Research 2021).

I am also a dedicated mentor and four former postdocs have already started independent faculty positions in France, UK, and Brazil.

B. Positions and Honors

2022 – Present	Full Professor, Department of Medical Biophysics, University of Toronto, Toronto, Canada
2017 – Present	Senior Scientist, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada
2017 – 2021	Associate Professor, Department of Medical Biophysics, University of Toronto, Toronto, Canada
2012 – 2017	Scientist, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada
2012 – 2017	Assistant Professor, Department of Medical Biophysics, University of Toronto, Toronto, Canada
2009 – 2012	Postdoctoral Fellow, Norris Comprehensive Cancer Center, University of Southern California (USC)

Other Experience and Professional Memberships

2021-2022	Education Committee for the AACR Annual Meeting 2022
2020	Chair of SAB, DNAMx. Inc
2019	Senior Advisory Committee, Princess Margaret Cancer Centre Research Institute
2014	Editorial Board member of Epigenomes Journal
2014	Co-organizer, Epigenetic Mechanisms in Cancer conference, Toronto
2013	Member, Canadian Cancer Society, Novel Therapeutics Panel (4x)
2013	Ad-hoc peer-reviewer for CIHR, Canada; National science Foundation (NSF), USA; Medical Research Council (MRC), UK; Cariplo Foundation, Italy; INSERM, France; and FAPESP, Brazil
2013-2015	Member, UofT Student ranking Committee, Department of Medical Biophysics (MBP), University of Toronto
2013-2015	Member of the Cancer Genomics Program (CGP) Immunotherapy and PDX Subcommittee, University Health Network
2013	Member of PMGC (Princess Margaret Genomics Centre) Advisory Board, University Health Network

Honors/Awards

Honors

2019	Elected membership in the 2019 cohort of the College of New Scholars, Artists and Scientists of the Royal Society of Canada
2019	Faculty member at Faculty Opinions (Former Faculty of 1000) at the Cancer Genomes & Epigenomes section. The faculty comprises peer-nominated, internationally-renowned researchers from across the world.
2016	Top 10 Research Impact Stories of 2015 by Canadian Cancer Society
2016	Top 10 Notable advances for 2015 by Nature Medicine
2012	Work featured on ASCO's "Clinical Cancer Advances 2012: ASCO's Annual Report on Progress Against Cancer" as a major advance in Tumor Biology and Developmental Therapeutics

Awards

2022	**2022 Recipient of the AACR-Waun Ki Hong Award for Outstanding Achievement in Translational and Clinical Cancer Research**. This award recognizes *'a worthy cancer researcher such as yourself who has conducted highly meritorious translational and clinical cancer research anywhere in the world and who has not yet reached 51 years of age at the time of the award presentation'.*
2021	**UHN 2021 Local Impact Awards - Commercialization Award**: Winner of the Team Award with partner Dr. Scott Bratman
2021	**Recipient of UHN's 18th annual Inventor of the Year Award** (Co-awardee Dr. Scott Bratman) for their work on defining the generation of cancer diagnostics.
2019	**2018 Till and McCulloch Paper of the Year Award** - translational award for your publication "Sensitive tumour detection and classification using plasma cell-free DNA methylomes" published in Nature.
2019	**The EACR's Top 10 Cancer Research Publications**. My Research (Shen et al., Nature 2018) was highlighted by the EACR's Top 10 Cancer Research Publications
2019	**The AAAS Martin And Rose Wachtel Cancer Research Award** (Honorable Mention) – American Association for the Advancement of Science. Total amount: $1,000 USD
2017	**Bernard and Francine Dorval Prize**. Canadian Cancer Society Research Institute Total amount: $10,000 CAD
2017	**Early Career Award in Cancer**. CIHR Institute of Cancer Researc (ICR) Total amount: $25,000 CAD
2016	**Canada Research Chair in Cancer Epigenetics and Epigenetic Therapy**. CIHR Total amount: $500,000 CAD
2016	**CIHR New Investigator Salary Award.** Total amount: $300,000 CAD
2016	**Helen M Cook Professorship**. Princess Margaret Foundation

Total amount: $1,000,000 CAD

2015 **Till and McCulloch Paper of the Year Award**. Princess Margaret Cancer Centre
Total amount: $1,000 CAD

C. Contributions to Science

Published work:

https://scholar.google.ca/citations?user=XImzWX0AAAAJ&hl=en

TEs dysregulation in cancer development and cancer therapy

a. Roulois D, Loo Yau H, Singhania R, Wang Y, Danesh A, Shen SY, Han H, Liang G, Jones PA, Pugh TJ, O'Brien C, **De Carvalho DD**. DNA-Demethylating Agents Target Colorectal Cancer Cells by Inducing Viral Mimicry by Endogenous Transcripts. **Cell** 2015 (PMID: 26317465).
b. Wanqiang Sheng, Martin W LaFleur, Thao H Nguyen, Sujun Chen, Ankur Chakravarthy, Jake Ryan Conway, Ying Li, Hao Chen, Henry Yang, Pang-Hung Hsu, Eliezer M Van Allen, Gordon J Freeman, **Daniel D De Carvalho**, Housheng Hansen He, Arlene H Sharpe, Yang Shi. LSD1 ablation stimulates anti-tumor immunity and enables checkpoint blockade. **Cell** 2018 (PMID: 29937226)
c. Charles A Ishak, Marie Classon, **Daniel D De Carvalho**. Deregulation of retroelements as an emerging therapeutic opportunity in cancer. **Trends in Cancer** 2018 (PMID: 30064665)
d. Brian Krug, Nicolas De Jay, Ashot S Harutyunyan, …, Josie Ursini-Siegel, **Daniel D De Carvalho**, Peter B Dirks, Peter W Lewis, Paolo Salomoni, Mathieu Lupien, Cheryl Arrowsmith, Paul F Lasko, Benjamin A Garcia, Claudia L Kleinman, Nada Jabado, Stephen C Mack. Pervasive H3K27 acetylation leads to ERV expression and a therapeutic vulnerability in H3K27M gliomas. **Cancer Cell** 2019 (PMID: 31085178)
e. Parinaz Mehdipour, Sajid A Marhon, Ilias Ettayebi, Ankur Chakravarthy, Amir Hosseini, Yadong Wang, Fabíola Attié de Castro, Helen Loo Yau, Charles Ishak, Sagi Abelson, Catherine A O'Brien, **Daniel D De Carvalho**. Epigenetic therapy induces transcription of inverted SINEs and ADAR1 dependency. **Nature** 2020 (PMID: 33087935)
f. Geneviève Deblois, Seyed Ali Madani Tonekaboni, …, Cheryl H Arrowsmith, **Daniel D De Carvalho**, Benjamin Haibe-Kains, Jason W Locasale, Morag Park, Mathieu Lupien. Epigenetic switch–induced viral mimicry evasion in chemotherapy-resistant breast cancer. **Cancer Discovery** 2020 (PMID: 32546577)
g. Raymond Chen, Charles A Ishak, **Daniel D De Carvalho**. Endogenous retroelements and the viral mimicry response in cancer therapy and cellular homeostasis. **Cancer Discovery** 2021 (PMID: 34649957)
h. Petr Šulc, Alexander Solovyov, Sajid A Marhon, Siyu Sun, John LaCava, Omar Abdel-Wahab, Nicolas Vabret, **Daniel D De Carvalho***, Rémi Monasson*, Simona Cocco*, Benjamin D Greenbaum*. Repeats Mimic Immunostimulatory Viral Features Across a Vast Evolutionary Landscape. **BioRxiv** 2021

Epigenomics-based Biomarkers for Cancer early detection, sub-classification and prognostic

a. Torchia J, . . . **De Carvalho DD***, Rutka JT*, Jabado N*, Huang A*. (116 authors total). Integrated (epi)-Genomic Analyses Identify Subgroup-Specific Therapeutic Targets in CNS Rhabdoid Tumors. **Cancer Cell** 2016 (PMID: 27960086).
b. Justin M Burgener, Ariana Rostami, **Daniel D De Carvalho***, Scott V Bratman*. Cell-free DNA as a post-treatment surveillance strategy: current status. **Seminars in Oncology** 2017 (PMID: 29580435)
c. Shen SY, Singhania R, Chakravarthy A, Fehringer G, Roehrl MHA, Chadwick D, Zuzarte PC, Borgida A, Li T, Kis O, Zhao Z, Spreafico A, Medina T, Wang Y, Roulois D, Ettayebi I, Murphy T, Arruda A, Liu J, Mansour M, McPherson JD, O'Brien C, Leighl N, Bedard PL, Fleshner N, Liu G, Minden MD, Gallinger S, Pugh TJ, Bratman SV, Hung RJ, and **De Carvalho DD**. Sensitive tumor detection and classification using methylome analysis of plasma DNA. **Nature** 2018 (PMID: 30429608)
d. Shu Yi Shen, Justin M Burgener, Scott V Bratman, **Daniel D De Carvalho**. Preparation of cfMeDIP-seq libraries for methylome profiling of plasma cell-free DNA. **Nature Protocols** 2019 (PMID: 31471598)
e. Farshad Nassiri, Ankur Chakravarthy, Shengrui Feng, Shu Yi Shen, Romina Nejad, Jeffrey A Zuccato, Mathew R Voisin, Vikas Patil, Craig Horbinski, Kenneth Aldape, Gelareh Zadeh, **Daniel D De Carvalho**. Detection and discrimination of intracranial tumors using plasma cell-free DNA methylomes. **Nature Medicine** 2020 (PMID: 32572265)
f. Pier Vitale Nuzzo, Jacob E Berchuck, Keegan Korthauer, Sandor Spisak, …, Rafael A Irizarry, Mark Pomerantz, **Daniel D De Carvalho***, Toni K Choueiri*, Matthew L Freedman*. Detection of renal cell carcinoma using plasma and urine cell-free DNA methylomes. **Nature Medicine** 2020 (PMID: 32572266)

g. Sujun Chen, Guanghui Zhu, Yue Yang, …, Michael Fraser, **Daniel D De Carvalho**, Paul C Boutros, Dolores Di Vizio, Zhou Jiang, Theodorus van der Kwast, Alejandro Berlin, Song Wu, Jianhua Wang, Housheng Hansen He, Shancheng Ren. Single-cell analysis reveals transcriptomic remodellings in distinct cell types that contribute to human prostate cancer progression. Nature Cell Biology 2021 (PMID: 33420488)
h. Jeffrey A Zuccato, Vikas Patil, Sheila Mansouri, …, Kenneth D Aldape, **Daniel D De Carvalho**, Gelareh Zadeh. DNA Methylation based prognostic subtypes of chordoma tumors in tissue and plasma. **Neuro-Oncology** 2021 (PMID: 34614192
i. Justin M Burgener, Jinfeng Zou, Zhen Zhao, …, Michael M Hoffman, **Daniel D De Carvalho*,** Scott V Bratman*. Tumor-naïve multimodal profiling of circulating tumor DNA in head and neck squamous cell carcinoma. **Clinical Cancer Research** 2021 (PMID: 34158359)

Epigenetics of the immune response

a. Benevides L, da Fonseca DM, Donate PB, Tiezzi DG, **De Carvalho DD**, de Andrade JM, Martins GA, Silva JS. IL17 Promotes Mammary Tumor Progression by Changing the Behavior of Tumor Cells and Eliciting Tumorigenic Neutrophils Recruitment. **Cancer Res**. 2015 (PMID: 26208902)
b. Rahul Shinde, Kebria Hezaveh, Marie Jo Halaby, …, Joan Wither, **Daniel D De Carvalho**, Tracy L McGaha. Apoptotic cell–induced AhR activity is required for immunological tolerance and suppression of systemic lupus erythematosus in mice and humans. **Nature Immunology** 2018 (PMID: 29760532)
c. Ankur Chakravarthy, Lubaba Khan, Nathan Peter Bensler, Pinaki Bose, **Daniel D De Carvalho**. TGF-β-associated extracellular matrix genes link cancer-associated fibroblasts to immune evasion and immunotherapy failure. **Nature Communications** 2018 (PMID: 30410077)
d. Peter A Jones, Hitoshi Ohtani, Ankur Chakravarthy, **Daniel D De Carvalho**. Epigenetic therapy in immune-oncology. **Nature Reviews Cancer** 2019 (PMID: 30723290)
e. Helen Loo Yau, Ilias Ettayebi, **Daniel D De Carvalho**. The cancer epigenome: exploiting its vulnerabilities for immunotherapy. **Trends in Cell Biology** 2019 (PMID: 30153961)
f. Marie Jo Halaby, Kebria Hezaveh, Sara Lamorte, …, Trevor J Pugh, **Daniel D De Carvalho**, Marcus O Butler, Pamela S Ohashi, David G Brooks, Tracy L McGaha. GCN2 drives macrophage and MDSC function and immunosuppression in the tumor microenvironment. **Science Immunology** 2019 (PMID: 31836669)
g. Kirsty Taylor, Helen Loo Yau, Ankur Chakravarthy, …, Trevor J Pugh, Pamela S Ohashi, Lillian L Siu, **Daniel D De Carvalho**. An open-label, phase II multicohort study of an oral hypomethylating agent CC-486 and durvalumab in advanced solid tumors. **Journal for immunotherapy of cancer** 2020 (PMID: 32753546)
h. Helen Loo Yau, Emma Bell, Ilias Ettayebi, …, Joaquín Arribas, John Stagg, David G Brooks, **Daniel D De Carvalho**. DNA hypomethylating agents increase activation and cytolytic activity of CD8+ T cells. **Molecular Cell** 2021 (PMID: 33609448
i. Helen Loo Yau, **Daniel D De Carvalho**. Measuring the effect of drug treatments on primary human CD8+ T cell activation and cytolytic potential. **Star Protocols** 2021 (PMID: 34095863)

D. Additional Information: Research Support and/or Scholastic Performance

Terry Fox Research Institute De Carvalho (Co-PI) Oct. 2020 - Sep. 2026
The Determinants of Stemness that underlie high risk or relapse disease - Project 3 (Understanding, targeting, and monitoring cancer stemness and drug tolerant persistent states in colorectal cancer and beyond)
Main Objective: The overall goals of my project are to understand the biology; identify drug targets; and develop biomarkers to monitor cancer stemness and drug persistence states in colorectal cancer specifically and across different cancer types as part of this TFRI program.

Canadian Institutes for Health Research De Carvalho (PI) Oct. 2019 - Sep. 2024
Viral mimicry tolerance as a mechanism of early tumor immune invasion
Main objective: The main goal of our proposal is to inform approaches that will improve immunotherapy responses and cancer outcomes, particularly for ovarian cancer.

Ontario Institute for Cancer Research (OICR) De Carvalho (Co-PI) Apr. 2017 - Mar. 2021
OICR TRI - Ovarian Cancer Translational Research Initiative

Main Objective: We aim to develop predictive and pharmacodynamic biomarkers to impact therapeutic strategies to improve precision and outcome.

Ontario Institute for Cancer Research (OICR) De Carvalho (Co-PI) Apr. 2017 - Mar. 2021
Acute Leukemia Translational Research Initiative
Main Objective: The long-term goal is to isolate and characterize, from within the diagnostic sample, the subset of cells that are destined to survive initial therapy and contribute to generating the eventual AML relapse.

Canadian Institutes for Health Research De Carvalho (PI) Jul. 2016 – Jun. 2021
Epigenetic Approaches to Enhance Cancer Immunotherapy and to Target Cancer Initiating Cells.
Main Objective: Dissect the molecular mechanisms of how DNA demethylating agents increase anti-tumour immune responses and decrease tumour cell intrinsic self-renewal
Outline of Methodology: This project will use cell lines, PDX, organoids and syngeneic mice models for colorectal cancer and human derived T cells.

NSERC – Discovery Grant De Carvalho (PI) Apr. 2015 - Mar. 2023
Understanding the molecular mechanisms of Polycomb recruitment in ES cells and during cellular differentiation
Main Objective: The goal of this project is to generate maps of chromatin modifications during ES cell differentiation to understand the basic mechanisms recruiting chromatin modifiers to specific genomic coordinates.