

Issam Ben-Sahra, Ph.D.

CONTACT INFORMATION

Business Address: Northwestern University, Feinberg School of Medicine, 303 East Superior Street, Chicago, IL, 60611
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EDUCATION

Ph.D.	December 2010	University of Nice Côte d'Azur (France)	Cellular and Molecular Biology
Master	June 2007	University of Nice Cote d'Azur (France)	Genetics, Immunity and Development
Bachelor	June 2005	University of Nice Côte d'Azur (France)	Life Sciences

TRAINING

Jan-June 2007 Research Intern

INSERM unit 526 directed by Dr. Patrick Auberger
Project: Impact and role of AMPK in cell death and differentiation of Chronic Myelogenous Leukemia (CML) cells
Supervisor: Prof. Patrick Auberger

Jan-June 2006 Research Intern

INSERM unit 568 directed by Dr. Yannick Le Marchand-Brustel
Project: Effect of adipokines on prostate cancer cell growth.
Supervisor: Prof. Frédéric Bost

ACADEMIC APPOINTMENTS

09/2023-Present	Associate Professor of Biochemistry and Molecular Genetics Department of Biochemistry and Molecular Genetics Northwestern University Feinberg School of Medicine (Chicago, IL, USA)
01/2017-08/2023	Assistant Professor of Biochemistry and Molecular Genetics Department of Biochemistry and Molecular Genetics Northwestern University Feinberg School of Medicine (Chicago, IL, USA)
02/2011-12/2016	Postdoctoral Research Fellow Laboratory of Dr. Brendan Manning Department of Genetics & Complex Diseases Harvard T.H. Chan School of Public Health (Boston, MA, USA) Project: Role of mTORC1 in the regulation of cellular metabolism
09/2007-12/2010	Doctoral Research in the Laboratory INSERM U895 (now U1065) Centre Méditerranéen de Médecine Moléculaire (Nice, France) Thesis advisor: Prof. Frédéric Bost Thesis project: Metabolism and Cancer: Targeting cancer cell metabolism with metabolic stress inducing agents

HONORS AND AWARDS

- Elected Society Memberships

2019: William Guy Forbeck Scholar Award

2019: American Association for Cancer Research (AACR) (Member ID: 1060269)

- International/National/Regional

2021: Rising Stars of Cancer Metabolism and Signaling, New York Academy of Sciences

2017: LAM Foundation Career Development Award

2015: NIH K99/R00 Pathway to Independence Award (K99CA194192/ R00CA194192)

2012-2015: Postdoctoral Research Award, LAM Foundation
 2011: Young Scientist Award, Philippe Foundation
 2011: Young Scientist Award, Bettencourt-Shueller Foundation
 2011-2012: Award Recipient, Association pour la Recherche sur le Cancer Fellow

INTERNAL INSTITUTIONAL SERVICE

Member of the Radiation Safety Committee (RSC) at Northwestern University since September 2019.

LEADERSHIP POSITION

July 2023- **Program Co-leader at the Robert H. Lurie Cancer Center.**

With Drs. Navdeep Chandel and Curt Horvath, Dr. Ben-Sahra co-leads the Membranes, Organelles, & Metabolism (MOM) program.

MEMBER OF THESIS COMMITTEES:

Student Names	Thesis title	Institution	PhD Advisor	Date of Defense
Jay Daniels	Molecular drivers of CTCL and the regulation of T cell exhaustion	Northwestern University	Jaehyuk Choi	06/09/2022
Ram Prosad Chakrabarty	Biology of L-2-hydroxyglutarate	Northwestern University	Navdeep Chandel	Not yet
Corey Kennelly	Elucidating the role of the nucleotide salvage pathway in biofilm regulation in <i>Pseudomonas aeruginosa</i>	Northwestern University	Arthur Prindle	Not yet
Christian Marinaccio	Myeloproliferative Neoplasms: From Biology to Targeted Therapeutics	Northwestern University	John Crispino	Mar-21
Marwa Zerhouni	Resistance mechanisms to targeted therapies in metastatic melanoma and myelodysplastic syndromes	University of Nice, France	Patrick Auberger	7/7/2020
Ngoc Khac Linh Tran	Combination of Metformin and Valproic Acid For Prostate Cancer Treatment	Flinder University, Australia		7/1/2017
Claire Chaikin	Understanding the role of molecular clock transcription factor, BMAL1, in regulating glucose metabolism during diet-induced obesity	Northwestern University	Clara Peek	Not yet
Austin Klein	Elucidate the effects of various stress on cellular proteostasis through chemical-genetic screening approaches	Northwestern University	Marc Mendillo	Not yet

TEACHING ASSIGNMENTS:

Fall 2017:

Program	Type	Title	Audience
2017FA_IGP_485-0_SEC1	Data Analysis	Metabolomics	Biomedical Researchers

Fall 2018:

Program	Type	Lecture Title	Audience
2018FA_IGP_401-0_SEC20	Biochemistry I	Basics of cellular metabolism	DGP students
2018FA_IGP_401-0_SEC20	Biochemistry I	Cancer metabolism	DGP students
2018FA_IGP_485-0_SEC1 Data	Data Analysis	Metabolomics	Biomedical Researchers

Fall 2019:

Program	Type	Lecture Title	Audience
2019FA_IGP_401-0_SEC20	Biochemistry I	Basics of cellular metabolism	DGP students
2019FA_IGP_401-0_SEC20	Biochemistry I	Cancer metabolism	DGP students
2019FA_IGP_485-0_SEC1 Data	Data Analysis	Metabolomics	Biomedical Researchers

Fall 2020:

Program	Type	Lecture Title	Audience
2020FA_IGP_401-0_SEC20	Biochemistry I	Basics of cellular metabolism	DGP students
2020FA_IGP_401-0_SEC20	Biochemistry I	Cancer metabolism	DGP students
2020FA_IGP_401-0_SEC20	Biochemistry I	mTOR biology	DGP students
2020FA_IGP_485-0_SEC1 Data	Data Analysis	Metabolomics	Biomedical Researchers

Fall 2021:

Program	Type	Lecture Title	Audience
2021FA_IGP_401-0_SEC20	Biochemistry I	Basics of cellular metabolism	DGP students
2021FA_IGP_401-0_SEC20	Biochemistry I	Cancer metabolism	DGP students
2021FA_IGP_401-0_SEC20	Biochemistry I	mTOR biology	DGP students
2021FA_IGP_485-0_SEC1 Data	Data Analysis	Metabolomics	Biomedical Researchers

Fall 2022/Winter2023:

Program	Type	Lecture Title	Audience
Fall 2022			
2022FA_IGP_401-0_SEC20	Biochemistry I	Basics of cellular metabolism	DGP students
2022FA_IGP_401-0_SEC20	Biochemistry I	Cancer metabolism	DGP students
2022FA_IGP_401-0_SEC20	Biochemistry I	mTOR biology	DGP students
Winter 2023			
2023 Carcinogenesis Course	Carcinogenesis course	Paper discussion/Grant proposal	DGP students
Spring 2023			
2023FA_IGP_485-0_SEC1 Data	Data Analysis	Metabolomics	Biomedical Researchers

MANUSCRIPT REVIEW RESPONSIBILITIES

Ad Hoc Reviewer for:

Science

Nature

Cell

Nature Metabolism

Cell Metabolism

Molecular Cell

Nature Communications

Nature Cancer

Science Advances

Cell Reports

Journal of Clinical Investigation (JCI)

Science Immunology

Blood

Blood Advances

Cancer Research

Cancer Discovery

Trends in Cancer

Clinical Cancer Research

Oncogene

EMBO reports

Molecular Metabolism

Redox Biology

iScience
Cell Death and Disease
Cancer & Metabolism
Cell Chemical Biology
Cancers
PLoS Genetics
The Plant Cell

GRANT REVIEW RESPONSIBILITIES

2019: Michigan Nutrition and Obesity Research Center (MNORC) Pilot/Feasibility Study Grant Application
2020: Cancer Research UK Program Grant
2020: H Foundation Award
2021: National Agency for Research (France)
2022: INSERM ITMO Cancer (France)

GRANTS AND SPONSORED AWARDS

-Current:

Agency: Northwestern University/Brain SPORE Developmental Research

ID: P50CA221747; SPORE for Translational Approaches to Brain Cancer

Title: Enhancing Therapeutic Strategies: Targeting the RAS-ERK Pathway and De Novo Purine Synthesis to Combat Glioblastoma

Role on project: PI

Total costs for project period: \$50,000

Project period: 08/01/2023-07/31/2024

Agency: American Cancer Society (ACS)

ID/Award Number: 1039959/DBG-23-1039959-01-TBE

Title: Developing PROMIS: The blueprint of human proteome-metabolome interactions in cancers

Role on project: PI

Total costs for project period: \$300,000

Project period: 07/01/2023-06/30/2025

Agency: American Cancer Society (ACS)

ID: GMO 230110 PO 0000002901/RSG-22-177-01-TBE (Hoxhaj)

Title: Regulation of cancer cell migration through the purine-dependent control of serine synthesis

Role on project: Co-PI

Total costs for project period: \$200,000

Project period: 01/01/2023-12/31/2026

Agency: National Institutes of Health (NIH)

ID#: R01GM143334-01

Title: Control of RNA methylation by growth signals through the mTORC1 pathway

Principal Investigator: Ben-Sahra

Role on project: PI

Percent effort: 20%

Direct costs per year: \$200,000

Total costs for project period: \$800,000

Project period: 09/01/2021-05/31/2025

Agency: National Institutes of Health (NIH)

ID#: R01GM135587-02

Title: Regulation of de novo purine synthesis by the MAPK/ERK pathway

Principal Investigator: Ben-Sahra

Role on project: PI

Percent effort: 25%
Direct costs per year: \$210,000
Total costs for project period: \$1,050,000
Project period: 01/01/2020-12/31/2024

Agency: **National Institutes of Health (NIH)**

R01-GM143638-1 (Foltz) 07/01/21 - 6/30/26 1.80 calendar

NIH \$20,191 (PI support only)

Histone chaperone networks for new and evicted histones

Our work proposed in this application will define, for the first time, differential processes that regulate fate of new and pre-existing histones and provide a new paradigm for coordinated metabolic control.

Percent effort: 15%

Project period: 09/01/2021-12/31/2026

Role: Co-I

Agency: **National Institutes of Health (NIH)**

ID#: R01NS112856-02

Title: Role of purine metabolism in chemoresistance

Principal Investigator: Ahmed (Northwestern University)

Role on project: Co-I

Percent effort: 15%

Direct costs per year: \$80,000

Total costs for project period: \$400,000

Project period: 07/01/2019-06/30/2024

Agency: **LAM Foundation - Established Investigator Award**

ID#: LAM0151E01-22

Title: The TSC-mTORC1 Network Controls Bicarbonate Uptake to Support Cell Growth

Principal Investigator: Ben-Sahra

Role on project: PI

Percent effort: 5%

Direct costs per year: \$50,000

Total costs for project period: \$150,000

Project period: 03/01/2022-02/14/2025

-Completed:

Agency: **Reaumont Foundation**

ID#: NA

Title: KIAA1522 controls mTORC2 signaling downstream of KRAS in pancreatic cancer

Principal Investigator: Ben-Sahra

Role on project: PI

Percent effort: 0%

Direct costs per year: \$7,500

Total costs for project period: \$15,000

Project period: 02/15/2021-02/16/2023

Agency: **Memorial Hospital Grant (Lynn Sage)**

ID#: NA

Title: Understanding the impact of the Oncogenic Signaling Network on Cellular Metabolic Network in Human Breast Cancers

Principal Investigator: Ben-Sahra

Role on project: PI

Percent effort: 0.8%

Direct costs per year: \$50,000

Total costs for project period: \$50,000
Project period: 09/01/2017-08/31/2020

Agency: **LAM Foundation Career Development Award**

ID#: LAM0127C01-18 / NU #SP0046064

Title: Defining the mTORC1-dependent signaling mechanisms mediating epigenetic modifications

Principal Investigator: Ben-Sahra

Role on project: PI

Percent effort: 10%

Direct costs per year: \$60,000

Total costs for project period: \$180,000

Project period: 01/14/2018-03/31/2021

Agency: **National Institutes of Health (NIH)**

ID#: 5R00CA194192-04

Title: Linking oncogenic signaling to tumor metabolism

Principal Investigator: Ben-Sahra

Role on project: PI

Percent effort: 75%

Direct costs per year: \$160,423

Total costs for project period: \$481,269.00

Project period: 07/11/2019-12/31/2019

Agency: **National Institutes of Health (NIH)**

ID#: 1K99CA194192-01

Title: Linking oncogenic signaling to tumor metabolism

Principal Investigator: Ben-Sahra

Role on project: PI

Percent effort: 75%

Direct costs per year: \$97,252

Total costs for project period: \$97,252

Project period: 08/17/2015-12/31/2016

INVITED TALKS

A. International/National

Jan 2018: Keystone Symposia – Tumor Metabolism (A5), Snowbird Resort • Snowbird, Utah, USA (Invited Speaker)

Oct 2018: Midwest Metabolism Meeting, University of Notre Dame, OH, USA (Invited Speaker)

Nov 2018: Invited by Dr. Costas Lyssiotis to give the Metabolism and Diseases Seminar series at University of Michigan, MI.

Apr 2019: Invited by Dr. David Plas to give the Vontz Center Cancer Seminar series at the University of Cincinnati, OH.

Oct 2019: Invited by Dr. Taro Hitosugi to give the Molecular Pharmacology and Experimental Therapeutics Seminar series at the Mayo Clinic, Rochester, MN.

Nov 2019: William Guy Forbeck Focus Meeting, Geneva National, Lake Geneva, WI (Invited Speaker)

Apr 2019: 3rd edition of Metabolism & Cancer, Marseille, France (Invited Speaker)

Feb 2020: Invited by Dr. Philip Howe to give a seminar for the Molecular & Cellular Biology and Pathobiology Program with Pharmacology, MUSC, Charleston, SC.

Apr 2020: Invited by Dr. Philip White to present virtually a seminar for the Metabolic Physiology in Isolation seminar series #METPHYS2020. <https://sites.google.com/view/whitemcgarrahlab/metphys2020>

Apr 2021: Rising Stars of Cancer Metabolism and Signaling, New York Academy of Sciences, NY. Selected as a rising star speaker (Virtual talk).

Feb 2023: Invited by Dr. Anthony Covarrubias to give a seminar for the University of California, Los Angeles (UCLA), Los Angeles, CA.

Mar 2023: Invited by Dr. Rushika Perera to give a seminar for the Cancer Center Friday Seminar Series at University of California, San Francisco (UCSF), San Francisco, CA.

B. Local

Feb 2019: Invited by Dr. Bryan Laden to give the Endo's Diabetes & Obesity seminar series at the University of Illinois at Chicago, IL.

Feb 2020: Invited by Dr. Matthew Brady to give the Endocrinology, Diabetes and Metabolism Seminar series at the University of Chicago, IL.

Mar 2022: Invited by a graduate student panel led by Mr. Ahmed Magdy to give the Biochemistry and Molecular Genetics Seminar series at the University of Illinois at Chicago, IL.

Dec 2022: Invited by Dr. Jason Cantor to give the Metabolism Colloquium seminar at the Morgridge Institute for Research.

PEER-REVIEWED PUBLICATIONS

Zhao Z, Cao K, Watanabe J, Philips CN, Zeidner JM, Ishi Y, Wang Q, Gold SR, Junkins K, Bartom ET, Yue F, Chandel NS, Hashizume R, **Ben-Sahra I**, Shilatifard A. Therapeutic targeting of metabolic vulnerabilities in cancers with MLL3/4-COMPASS epigenetic regulator mutations. *J Clin Invest*. 2023 Jul 3;133(13):e169993.

Perrault EN, Shireman JM, Ali ES, Lin P, Preddy I, Park C, Budhiraja S, Baisiwala S, Dixit K, James CD, Heiland DH, **Ben-Sahra I**, Pott S, Basu A, Miska J, Ahmed AU. Ribonucleotide reductase regulatory subunit M2 drives glioblastoma TMZ resistance through modulation of dNTP production. *Science Advances*. 2023 May 19;9(20):eade7236. doi: 10.1126/sciadv.ade7236.

Sawicki KT, Ning H, Allen NB, Carnethon MR, Wallia A, Otvos JD, **Ben-Sahra I**, McNally EM, Snell-Bergeon JK, Wilkins JT. Longitudinal trajectories of branched chain amino acids through young adulthood and diabetes in later life. *JCI Insight*. 2023 Apr 24;8(8):e166956. doi: 10.1172/jci.insight.166956.

Ali ES, **Ben-Sahra I**. Regulation of nucleotide metabolism in cancers and immune disorders. *Trends Cell Biol*. 2023 Mar 24:S0962-8924(23)00044-2. doi: 10.1016/j.tcb.2023.03.003.

Ma Q, Yang Q, Xu J, Sellers HG, Brown ZL, Liu Z, Bordan Z, Shi X, Zhao D, Cai Y, Pareek V, Zhang C, Wu G, Dong Z, Verin AD, Gan L, Du Q, Benkovic SJ, Xu S, Asara JM, **Ben-Sahra I**, Barman S, Su Y, Fulton DJR, Huo Y. Purine synthesis suppression reduces the development and progression of pulmonary hypertension in rodent models. *Eur Heart J*. 2023 Jan 31;ehad044. doi: 10.1093/eurheartj/ehad044.

Jin Q, Gutierrez Diaz B, Pieters T, Zhou Y, Narang S, Fijalkowski I, Borin C, Van Laere J, Payton M, Cho BK, Han C, Sun L, Serafin V, Yacu G, Von Loocke W, Basso G, Veltri G, Dreveny I, **Ben-Sahra I**, Goo YA, Safgren SL, Tsai YC, Bornhauser B, Suraneni PK, Gaspar-Maia A, Kandela I, Van Vlierberghe P, Crispino JD, Tsigirigos A, Ntziachristos P. Oncogenic deubiquitination controls tyrosine kinase signaling and therapy response in acute lymphoblastic leukemia. *Science Advances*. 2022 Dec 9;8(49):eabq8437.

Ma Q, Yang Q, Xu J, Zhang X, Kim D, Liu Z, Da Q, Mao X, Zhou Y, Cai Y, Pareek V, Kim HW, Wu G, Dong Z, Song WL, Gan L, Zhang C, Hong M, Benkovic SJ, Weintraub NL, Fulton D Jr, Asara JM, **Ben-Sahra I**, Huo Y. ATIC-Associated De Novo Purine Synthesis Is Critically Involved in Proliferative Arterial Disease. *Circulation*. 2022 Nov 8;146(19):1444-1460.

Khan MW, Terry AR, Priyadarshini M, Ilievski V, Farooq Z, Guzman G, Cordoba-Chacon J, **Ben-Sahra I**, Wicksteed B, Layden BT. The hexokinase "HKDC1" interaction with the mitochondria is essential for liver cancer progression. *Cell Death Dis*. 2022 Jul 28;13(7):660.

Amici DR, Ansel DJ, Metz KA, Smith RS, Phoumyvong CM, Gayatri S, Chamera T, Edwards SL, O'Hara BP, Srivastava S, Brockway S, Takagishi SR, Cho BK, Goo YA, Kelleher NL, **Ben-Sahra I**, Foltz DR, Li J, Mendillo ML. C16orf72/HAPSTR1 is a molecular rheostat in an integrated network of stress response pathways. *Proc Natl Acad Sci U S A*. 2022 Jul 5;119(27):e2111262119.

Calhoun JD, Aziz MC, Happ HC, Gunti J, Gleason C, Mohamed N, Zeng K, Hiller M, Bryant E, Mithal DS, Bellinski I, Kinsley L, Grimm M, Schwaibold EMC, Smith-Hicks C, Chassevent A, Scala M, Accogli A, Torella A, Striano P, Capra

V, Bird LM, **Ben-Sahra I**, Ekhilevich N, Hershkovitz T, Weiss K, Millichap J, Gerard EE, Carvill GL. mTORC1 functional assay reveals SZT2 loss-of-function variants and a founder in-frame deletion. *Brain*. 2022 Jun 30;145(6):1939-1948.

Ali ES, Lipońska A, O'Hara BP, Amici DR, Torno MD, Gao P, Asara JM, Yap MF, Mendillo ML, and **Ben-Sahra I**. The mTORC1-SLC4A7 axis stimulates bicarbonate import to enhance de novo nucleotide synthesis. *Molecular Cell*. 2022 Jun 24:S1097-2765(22)00544-5.

- This article was highlighted in *Molecular Cell* by Dr. Seth Parker's group.
<https://doi.org/10.1016/j.molcel.2022.08.010>

Soflaee MH, Kesavan R, Sahu U, Tasdogan A, Villa E, Djabari Z, Cai F, Tran DH, Vu HS, Ali ES, Rion H, O'Hara BP, Kelekar S, Hallett JH, Martin M, Mathews TP, Gao P, Asara JM, Manning BD*, **Ben-Sahra I***, Hoxhaj G*. Purine nucleotide depletion prompts cell migration by stimulating the serine synthesis pathway. *Nature Communications*. 2022 May 16;13(1):2698. * Co-corresponding authors.

Kouzu H, Tatekoshi Y, Chang HC, Shapiro JS, McGee WA, De Jesus A, **Ben-Sahra I**, Arany Z, Leor J, Chen C, Blackshear PJ, Ardehali H. ZFP36L2 suppresses mTORc1 through a P53-dependent pathway to prevent peri-partum cardiomyopathy in mice. *J Clin Invest*. 2022 Mar 22:e154491.

De Jesus A, Keyhani-Nejad F, Pusec CM, Goodman L, Geier JA, Stoolman JS, Stanczyk PJ, Nguyen T, Xu K, Suresh KV, Chen Y, Rodriguez AE, Shapiro JS, Chang HC, Chen C, Shah KP, **Ben-Sahra I**, Layden BT, Chandel NS, Weinberg SE, Ardehali H. Hexokinase 1 cellular localization regulates the metabolic fate of glucose. *Molecular Cell*. 2022 Mar 14:S1097-2765(22)00166-6.

Byles V, Cormerais Y, Kalafut K, Barrera V, Hughes Hallett JE, Sui SH, Asara JM, Adams CM, Hoxhaj G, **Ben-Sahra I**, Manning BD. Hepatic mTORC1 signaling activates ATF4 as part of its metabolic response to feeding and insulin. *Molecular Metabolism*. 2021 Jul 23;53:101309.

Sawicki KT, **Ben-Sahra I**, McNally EM. SGLT2 Inhibition on Cardiac Mitochondrial Function: Searching for a Sweet Spot. *J Am Heart Assoc*. 2021 Jul 6;10(13):e021949.

Zerhouni M, Martin AR, Furstoss N, Gutierrez VS, Jaune E, Tekaya N, Beranger GE, Abbe P, Regazzetti C, Amdouni H, Driowya M, Dubreuil P, Luciano F, Jacquelin A, Tulic MK, Cluzeau T, O'Hara BP, **Ben-Sahra I**, Passeron T, Benhida R, Robert G, Auberger P, Rocchi S. Dual Covalent Inhibition of PKM and IMPDH Targets Metabolism in Cutaneous Metastatic Melanoma. *Cancer Research*. 2021 Jul 15;81(14):3806-3821.

Shireman JM, Atashi F, Lee G, Ali ES, Saathoff MR, Park CH, Savchuk S, Baisiwala S, Miska J, Lesniak MS, James CD, Stupp R, Kumthekar P, Horbinski CM, **Ben-Sahra I**, Ahmed AU. De novo purine biosynthesis is a major driver of chemoresistance in glioblastoma. *Brain*. 2021 Apr 14:awab020.

Villa E, Sahu U, O'Hara BP, Ali ES, Helmin KA, Asara JM, Gao P, Singer BD, **Ben-Sahra I**. mTORC1 stimulates cell growth through SAM synthesis and m6A mRNA-dependent control of protein synthesis. *Molecular Cell*. 2021 Mar 17:S1097-2765(21)00177-5.

- This article was highlighted in *Molecular Cell* by Michael N. Hall's group:
<https://doi.org/10.1016/j.molcel.2021.04.020>

Srivastava S, Sahu U, Zhou Y, Hogan AK, Sathyan KM, Bodner J, Huang J, Wong KA, Khalatyan N, Savas JN, Ntziachristos P, **Ben-Sahra I**, Foltz DR. NOTCH1-driven UBR7 stimulates nucleotide biosynthesis to promote T cell acute lymphoblastic leukemia. *Science Advances*. 2021 Jan 27;7(5):eabc9781

Covarrubias AJ, Kale A, Perrone R, Lopez-Dominguez JA, Pisco AO, Kasler HG, Schmidt MS, Heckenbach I, Kwok R, Wiley CD, Wong HS, Gibbs E, Iyer SS, Basisty N, Wu Q, Kim IJ, Silva E, Vitangcol K, Shin KO, Lee YM, Riley R, **Ben-Sahra I**, Ott M, Schilling B, Scheibye-Knudsen M, Ishihara K, Quake SR, Newman J, Brenner C, Campisi J, Verdin E. Senescent cells promote tissue NAD⁺ decline during ageing via the activation of CD38⁺ macrophages. *Nat Metab*. 2021 Jan;3(1):120-121.

Ali ES, Sahu U, Villa E, O'Hara BP, Gao P, Beaudet P, Wood AW, Asara JM, **Ben-Sahra I**. ERK2 Phosphorylates PFAS to Mediate Posttranslational Control of De Novo Purine Synthesis. *Molecular Cell*. 2020 May 28;S1097-2765(20)30302-6.

Villa E, Ali ES, Sahu U, **Ben-Sahra I**. Cancer Cells Tune the Signaling Pathways to Empower de Novo Synthesis of Nucleotides. *Cancers* (Basel). 2019 May 17;11(5). pii: E688. doi: 10.3390/cancers11050688.

Kaminski L, Torrino S, Dufies M, Djabari Z, Haider R, Roustan FR, Jaune E, Laurent K, Nottet N, Michiels JF, Gesson M, Rocchi S, Mazure NM, Durand M, Tanti JF, Ambrosetti D, Clavel S, **Ben-Sahra I**, Bost F. PGC-1 α inhibits polyamine synthesis to suppress prostate cancer aggressiveness. *Cancer Res*. 2019 May 7. pii: canres.2043.2018.

Hoxhaj G, **Ben-Sahra I**, Lockwood SE, Timson RC, Byles V, Henning GT, Gao P, Selfors LM, Asara JM, Manning BD. Direct stimulation of NADP⁺ synthesis through Akt-mediated phosphorylation of NAD kinase. *Science*. 2019 Mar 8;363(6431):1088-1092

Yuan M, Kremer DM, Huang H, Breitkopf SB, **Ben-Sahra I**, Manning BD, Lyssiotis CA, Asara JM. Ex vivo and in vivo stable isotope labelling of central carbon metabolism and related pathways with analysis by LC-MS/MS. *Nat Protoc*. 2019 Feb;14(2):313-330.

Zhang S, Weinberg S, DeBerge M, Gainullina A, Schipma M, Kinchen JM, **Ben-Sahra I**, Gius DR, Yvan-Charvet L, Chandel NS, Schumacker PT, Thorp EB. Efferocytosis Fuels Requirements of Fatty Acid Oxidation and the Electron Transport Chain to Polarize Macrophages for Tissue Repair. *Cell Metab*. 2019 Feb 5;29(2):443-456.e5.

Sato T, Chang HC, Bayeva M, Shapiro JS, Ramos-Alonso L, Kouzu H, Jiang X, Liu T, Yar S, Sawicki KT, Chen C, Martínez-Pastor MT, Stumpo DJ, Schumacker PT, Blackshear PJ, **Ben-Sahra I**, Puig S, Ardehali H. mRNA-binding protein tristetraprolin is essential for cardiac response to iron deficiency by regulating mitochondrial function. *Proc Natl Acad Sci U S A*. 2018 Jul 3;115(27):E6291-E6300.

Longchamp A, Mirabella T, Arduini A, MacArthur MR, Das A, Treviño-Villarreal JH, Hine C, **Ben-Sahra I**, Knudsen NH, Brace LE, Reynolds J, Mejia P, Tao M, Sharma G, Wang R, Corpataux JM, Haefliger JA, Ahn KH, Lee CH, Manning BD, Sinclair DA, Chen CS, Ozaki CK, Mitchell JR. Amino Acid Restriction Triggers Angiogenesis via GCN2/ATF4 Regulation of VEGF and H₂S Production. *Cell*. 2018 Mar 22;173(1):117-129.e14.

Hoxhaj G, Hughes-Hallett J, Timson RC, Ilagan E, Yuan M, Asara JM, **Ben-Sahra I**, Manning BD. The mTORC1 Signaling Network Senses Changes in Cellular Purine Nucleotide Levels. *Cell Rep*. 2017 Oct 31;21(5):1331-1346.

Lam HC, Liu HJ, Baglini CV, Filippakis H, Alesi N, Nijmeh J, Du H, Lope AL, Cottrill KA, Handen A, Asara JM, Kwiatkowski DJ, **Ben-Sahra I**, Oldham WM, Chan SY, Henske EP. Rapamycin-induced miR-21 promotes mitochondrial homeostasis and adaptation in mTORC1 activated cells. *Oncotarget*. 2017 Aug 4;8(39):64714-64727.

Loubiere C, Clavel S, Gilleron J, Harisseh R, Fauconnier J, **Ben-Sahra I**, Kaminski L, Laurent K, Herkenne S, Lacas-Gervais S, Ambrosetti D, Alcor D, Rocchi S, Cormont M, Michiels JF, Mari B, Mazure NM, Scorrano L, Lacampagne A, Gharib A, Tanti JF, Bost F. The energy disruptor metformin targets mitochondrial integrity via modification of calcium flux in cancer cells. *Sci Rep*. 2017 Jul 11;7(1):5040.

Ben-Sahra I*, Manning BD*. mTORC1 signaling and the metabolic control of cell growth. *Curr Opin Cell Biol*. 2017 Apr 12;45:72-82. doi: 10.1016/j.ceb.2017.02.012. (*co-corresponding author).

Fenouille N, Bassil CF, **Ben-Sahra I**, Benajiba L, Alexe G, Ramos A, Pikman Y, Conway AS, Burgess MR, Li Q, Luciano F, Auberger P, Galinsky I, DeAngelo DJ, Stone RM, Zhang Y, Perkins AS, Shannon K, Hemann MT, Puissant A, Stegmaier K. The creatine kinase pathway is a metabolic vulnerability in EVI1-positive acute myeloid leukemia. *Nat Med*. 2017 Feb 13. doi: 10.1038/nm.4283.

Ben-Sahra I, Hoxhaj G, Ricoult SJ, Asara JM, Manning BD. mTORC1 induces *de Novo* Purine Synthesis Through Control of the Mitochondrial Tetrahydrofolate Cycle. *Science* 12 Feb 2016: Vol. 351, Issue 6274, pp. 728-733

Covarrubias AJ, Aksoylar HI, Yu J, Snyder NW, Worth AJ, Iyer S, Wang J, **Ben-Sahra I**, Byles V, Espinosa C, Manning BD, Zhang Y, Blair IA, and Horng T. The Akt-ACLY axis couples metabolic signals to histone acetylation and gene expression in M2 macrophages. *eLife*. 2016 Feb 19;5. pii: e11612. doi: 10.7554/eLife.11612.

Ricoult SJ, Yecies JL, **Ben-Sahra I**, Manning BD. Oncogenic PI3K and K-Ras stimulate *de novo* lipid synthesis through mTORC1 and SREBP. *Oncogene*. 2015 Jun 1. doi: 10.1038/onc.2015.179.

Liu XS, Haines JE, Mehanna EK, Genet MD, **Ben-Sahra I**, Asara JM, Manning BD, Yuan ZM. ZBTB7A acts as a tumor suppressor through the transcriptional repression of glycolysis. *Genes Dev*. 2014 Sep 1;28(17):1917-28. doi: 10.1101/gad.245910.114.

Rosilio C, **Ben-Sahra I**, Bost F, Peyron JF. Metformin: a metabolic disruptor and anti-diabetic drug to target human leukemia. *Cancer Lett*. 2014 May 1;346(2):188-96.

Lall R, Ganapathy S, Yang M, Xiao S, Xu T, Su H, Shadfan M, Asara JM, Ha CS, **Ben-Sahra I**, Manning BD, Little JB, Yuan ZM. Low-dose radiation exposure induces a HIF-1-mediated adaptive and protective metabolic response. *Cell Death Differ*. 2014 May; 21(5):836-44.

Howell JJ, Ricoult SJ, **Ben-Sahra I**, Manning BD. A growing role for mTOR in promoting anabolic metabolism. *Biochem Soc Trans*. 2013 Aug;41(4):906-12. doi: 10.1042/BST20130041.

Ben-Sahra I, Howell JJ, Asara JM, Manning BD. Stimulation of *de novo* pyrimidine synthesis by growth signaling through mTOR and S6K1. *Science*. 2013 Mar 15;339(6125):1323-8. doi: 10.1126/science.1228792. Epub 2013 Feb 21

- This article was highlighted in *Cell Metabolism* by John Blenis's group:
<https://doi.org/10.1016/j.molcel.2021.04.020>
- This article was highlighted in *Nature Cell Biology*:
<https://www.nature.com/articles/ncb2733>

Byles V, Covarrubias AJ, **Ben-Sahra I**, Lamming DW, Sabatini DM, Manning BD, Horng T. The TSC-mTOR pathway regulates macrophage polarization. *Nat Commun*. 2013;4:2834. doi: 10.1038/ncomms3834.

Rosilio C, Lounnas N, Nebout M, Imbert V, Hagenbeek T, Spits H, Asnafi V, Pontier-Bres R, Reverso J, Michiels JF, **Ben-Sahra I**, Bost F, Peyron JF. The metabolic perturbators metformin, phenformin and AICAR interfere with the growth and survival of murine PTEN-deficient T cell lymphomas and human T-ALL/T-LL cancer cells. *Cancer Lett*. 2013 Aug 9;336(1):114-26. doi: 10.1016/j.canlet.2013.04.015. Epub 2013 Apr 21.

Ben-Sahra I, Dirat B, Laurent K, Puissant A, Auberger P, Budanov A, Tanti JF, Bost F. Sestrin2 integrates Akt and mTOR signaling to protect cells against energetic stress-induced death. *Cell Death Differ*. 2013 Apr;20(4):611-9. doi: 10.1038/cdd.2012.157. Epub 2012 Dec 14.

Puissant A, Dufies M, Fenouille N, **Ben-Sahra I**, Jacquelin A, Robert G, Cluzeau T, Deckert M, Tichet M, Chéli Y, Cassuto JP, Raynaud S, Legros L, Pasquet JM, Mahon FX, Luciano F, Auberger P. Imatinib triggers mesenchymal-like conversion of CML cells associated with increased aggressiveness. *J Mol Cell Biol*. 2012 Aug; 4(4):207-20. doi: 10.1093/jmcb/mjs010. Epub 2012 Mar 31.

Bost F, **Ben-Sahra I**, Tanti JF. Prevention of mutagenesis: new potential mechanisms of metformin action in neoplastic cells. *Cancer Prev Res (Phila)*. 2012 Apr;5(4):503-6. doi: 10.1158/1940-6207.CAPR-12-0085.

Bost F, **Ben-Sahra I**, Le Marchand-Brustel Y, Tanti JF. Metformin and cancer therapy. *Curr Opin Oncol*. 2012 Jan;24(1):103-8. doi: 10.1097/CCO.0b013e32834d8155. Review.

Ben-Sahra I, Regazzetti C, Robert G, Laurent K, Le Marchand-Brustel Y, Auberger P, Tanti JF, Giorgetti-Peraldi S, Bost F. Metformin, independent of AMPK, induces mTOR inhibition and cell-cycle arrest through REDD1. *Cancer Res*. 2011 Jul 1;71(13):4366-72. doi: 10.1158/0008-5472.CAN-10-1769. Epub 2011 May 3.

Ben Sahra I, Tanti JF, Bost F. The combination of metformin and 2 deoxyglucose inhibits autophagy and induces AMPK-dependent apoptosis in prostate cancer cells. *Autophagy*. 2010 Jul 1;6(5).

Ben Sahra I, Laurent K, Giuliano S, Larbret F, Ponzio G, Gounon P, Le Marchand-Brustel Y, Giorgetti-Peraldi S, Cormont M, Bertolotto C, Deckert M, Auberger P, Tanti JF, Bost F. Targeting cancer cell metabolism: the combination of metformin and 2-deoxyglucose induces p53-dependent apoptosis in prostate cancer cells. *Cancer Res*. 2010 Mar 15;70(6):2465-75. doi: 10.1158/0008-5472.CAN-09-2782. Epub 2010 Mar 9.

Robert G, **Ben Sahra I**, Puissant A, Colosetti P, Belhacene N, Gounon P, Hofman P, Bost F, Cassuto JP, Auberger P. Acadesine kills chronic myelogenous leukemia (CML) cells through PKC-dependent induction of autophagic cell death. *PLoS One*. 2009 Nov 18;4(11):e7889. doi: 10.1371/journal.pone.0007889.

Regazzetti C, Peraldi P, Grémeaux T, Najem-Lendom R, **Ben-Sahra I**, Cormont M, Bost F, Le Marchand-Brustel Y, Tanti JF, Giorgetti-Peraldi S. Hypoxia decreases insulin signaling pathways in adipocytes. *Diabetes*. 2009 Jan;58(1):95-103. doi: 10.2337/db08-0457. Epub 2008 Nov 4.

Ben Sahra I, Laurent K, Loubat A, Giorgetti-Peraldi S, Colosetti P, Auberger P, Tanti JF, Le Marchand-Brustel Y, Bost F. The antidiabetic drug metformin exerts an antitumoral effect in vitro and in vivo through a decrease of cyclin D1 level. *Oncogene*. 2008 Jun 5;27(25):3576-86. doi: 10.1038/sj.onc.1211024. Epub 2008 Jan 21.

INVITED REVIEWS AND COMMENTARIES

Sahu U, **Ben-Sahra I**. The cell cycle loops UTP around CAD. *Nature Metabolism*. 2023 Feb;5(2):199-200.

Sahu U, **Ben-Sahra I**. GATOR2 rings GATOR1 to speak to mTORC1. *Molecular Cell*. 2023 Jan 5;83(1):6-8.

Villa E, **Ben-Sahra I**. ASS1igning purine dependency to cancer. *Nature Cancer* 1, 862–863 (2020).

Hoxhaj G*, Locasale JW*, **Ben-Sahra I***. A spoonful of DHAP keeps mTORC1 running on sugars. *Nature Metabolism*. 2020 Sep;2(9):801-802. doi: 10.1038/s42255-020-0246-1. * Co-corresponding authors.

Ben-Sahra I, Puissant A. HER2 Signaling Hijacks the Creatine Shuttle to Fuel Breast Cancer Cell Growth. *Cell Metab*. 2018 Dec 4;28(6):805-807.

CONFERENCE PROCEEDINGS

Jan 2008: World apoptosis Luxembourg (Selected oral presentation)

Mar 2008: Alfediam Bruxelles (Selected oral presentation)

Nov 2009: Molecular and cancer therapeutics Boston, MA, USA (Poster presentation)

Nov 2010: Metabolism and Cancer, IRB, Barcelona, (Poster presentation)

Nov 2011: Metabolism and Cancer, AACR, Baltimore, MD, USA

Apr 2013: LAM symposium, Cincinnati, OH, USA (Selected oral presentation)

Sept 2014: Metabolism and Cancer Conference, Nice, France (Selected oral presentation)

Oct 2014: Cancer Metabolism meeting, Discovery of Target, Boston, MA, USA (Selected Speaker)

Feb 2013: Keystone meeting Tumor Metabolism, Denver, Colorado, USA

Feb 2016: Keystone meeting “New Frontiers in Understanding Tumor Metabolism” Banff, Alberta, Canada

Mar 2017: Keystone meeting Tumor Metabolism: Mechanisms and Targets, Whistler, Canada

Jan 2018: Keystone Symposia – Tumor Metabolism (A5), Snowbird Resort • Snowbird, Utah, USA

Oct 2018: Midwest Metabolism Meeting, Notre Dame, OH, USA

Apr 2019: Metabolism and Cancer, Marseille, France

Nov 2019: Simpson Querrey Center for Epigenetics Meeting, Northwestern University, Chicago, IL, USA

Nov 2019: William Guy Forbeck Scholar Forum, Lake Geneva, WI, USA

Apr 2021: Rising Stars of Cancer Metabolism and Signaling, New York Academy of Sciences, NY, USA

MEDIA COVERAGE AND APPEARANCES

[Combining Epigenetic and Metabolic Approaches for Targeted Cancer Treatment](#)

Northwestern Medicine scientists have identified a novel vulnerability in a subset of genes commonly mutated in cancer, according to a study recently published in *The Journal of Clinical Investigation*.

[Investigators Identify Mechanisms Behind Chemotherapy Resistance](#)

A team led by Northwestern Medicine investigators have discovered novel cellular mechanisms that lead to chemotherapy resistance in recurrent glioblastoma, according to findings published in *Science Advances*.

[Investigators Explore Cellular Response to Stress](#)

Northwestern Medicine investigators have discovered novel mechanisms that regulate cellular stress response, according to findings published in the *Proceedings of the National Academy of Sciences*.

[Targeting Bicarbonate in Cancer](#)

Bicarbonate ions are required for cell growth in some cancers, according to a Northwestern Medicine study.

[Genetic Variants in Epilepsy Gene Identified](#)

Investigators have discovered a new method to determine whether individual genetic variants in the epilepsy-associated gene *SZT2* cause the neurodevelopmental disorder, according to a Northwestern Medicine study.

[Immunosuppression Drug Could Reduce Chemotherapy Resistance](#)

A drug currently used to prevent organ rejection in transplants could also reduce chemotherapy resistance in glioblastoma, according to a Northwestern Medicine study.

Selected for the *Molecular Cell* Cover (May 20th, 2021, issue)

http://eproof.dartmouthjournals.com/pdfproofing/molcel_81_10_4c.pdf

[Inhibiting SAM Biosynthesis to Slow Tumor Growth](#)

Inhibiting production of a key material produced by the mTOR pathway could slow tumor growth, according to a recent Northwestern Medicine study.

[Leukemia Hijacks Nucleotide Metabolism](#)

T-cell acute lymphoblastic leukemia hijacks a signaling pathway to produce nucleotides, a basic building block of life that fuels the growth and spread of the cancer, according to a recent study.

[2020: A Year of Groundbreaking Discoveries During a Pandemic](#)

Take a look back at a handful of groundbreaking research discoveries that marked one of, if not the most, unprecedented and transformative years for Feinberg.

[Cancer Cells Hijack Nucleotide Metabolism to Boost Cell Proliferation](#)

Mutations in the genes *RAS* and *RAF* allow cancer cells to create their own nucleotides, fueling cancer growth, according to a recent study published in *Molecular Cell*.

[Uncovering Mechanisms of Cellular Growth and Division](#)

A new study has uncovered a key mechanism underlying the control of a co-factor that is essential for all cells to grow and divide, and which may also play a key role in cancer cell growth.

[Scientists Discover New Heart Attack Repair Pathway](#)

Northwestern Medicine scientists have discovered a novel signaling pathway that promotes healing and tissue repair after heart attack, in a study published in *Cell Metabolism*.

[Cellular Mechanism Protects Organs During Iron Deficiency](#)

A protein called tristetraprolin is activated during iron deficiency, lowering iron usage and preventing mitochondrial dysfunction, according to a recent Northwestern Medicine study.

Virtual Seminar from Dr. Issam Ben-Sahra available on YouTube:

Metabolic Physiology in Isolation #METPHYS2020 DAY26, Issam Ben-Sahra, Northwestern University

<https://www.youtube.com/watch?v=SRMzqVJh33A&t=1097s>

The Ben-Sahra Lab runs a Twitter account and shares research discoveries with the scientific community and the lay audience:

Twitter Handle: @bensahralab

Home: <https://twitter.com/bensahralab>