

**Issam Ben-Sahra**

Department of Biochemistry and Molecular Genetics  
Northwestern University Feinberg School of Medicine  
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**CURRENT POSITION**

**01/2017-Present**      **Assistant Professor of Biochemistry and Molecular Genetics**  
Department of Biochemistry and Molecular Genetics  
Northwestern University Feinberg School of Medicine (Chicago, IL, USA)

**PREVIOUS POSITION**

**2011- 12/2016**      **Postdoctoral Research Fellow**  
Department of Genetics & Complex Diseases  
Harvard T.H. Chan School of Public Health (Boston, MA, USA)

**EDUCATION**

**2007-2010**      **PhD in Cellular and Molecular Biology**  
INSERM U895  
Centre Méditerranée de Médecine Moléculaire  
University of Nice, Sophia-Antipolis (France)

**2005-2007**      **Master Degree in Genetics, Immunity and Development**  
University of Nice, Sophia-Antipolis

**2004-2005**      **Bachelor Degree in Life Sciences**  
University of Nice, Sophia-Antipolis

**RESEARCH EXPERIENCE**

**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 nucleotide synthesis**

**09/2007-12/2010**      **Doctoral Research in the Laboratory INSERM U895 (now U1065)**  
Thesis adviser: Prof. Frédéric Bost  
**Thesis project: Metabolism and Cancer: Targeting cancer cell metabolism with metabolic stress inducing agents**

**Jan-June 2007**      **Research Assistant**  
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 Assistant**  
INSERM unit 568 directed by Dr. Yannick Le Marchand-Brustel  
**Project: Effect of adipokines on prostate cancer cell growth.**  
Supervisor: Prof. Frédéric Bost

### **HONORS AND AWARDS**

2019: William Guy Forbeck Scholar Award  
2017: LAM Foundation Career Development Award  
2015: 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  
2007-2010: Doctoral contract, funded by the French Ministry of Higher Education and Research

### **CURRENT FUNDING:**

NIH/NIGMS R01GM135587-01A1      \$210K/year      Jan 15<sup>th</sup> 2020 – Jan 15<sup>st</sup> 2025  
Role: PI

NIH/NINDS 1R01NS112856-01      \$80K/year      Sept 1<sup>st</sup> 2019 – Sept 1<sup>st</sup> 2024  
Role: Co-I

### **COMPLETED FUNDING:**

LAM Foundation Career Development Award      \$60K/year      Jan 1<sup>st</sup> 2018 – Jan 1<sup>st</sup> 2021  
Role: PI

Lynne Sage Cancer Research Foundation      \$50K      Oct 1<sup>st</sup> 2017 – Oct 1<sup>st</sup> 2018  
Role: PI

NIH/NCI 4R00CA194192      \$249K/year      Jan 1<sup>st</sup> 2017 – Jan 1<sup>st</sup> 2020  
Role: PI

**Postdoctoral Fellowships:**

NIH/NCI Pathway to Independence Award 1K99 CA194192-01	Aug 1 <sup>st</sup> 2015 – Jan 1 <sup>st</sup> 2017
LAM Foundation Postdoctoral Fellowship	Jan 1 <sup>st</sup> 2012 – Jan 1 <sup>st</sup> 2015
Association sur la recherche contre le cancer (ARC Foundation)	Feb 4 <sup>th</sup> 2011 – Feb 1 <sup>st</sup> 2012

**PUBLICATIONS**

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. doi: 10.1016/j.molcel.2021.03.009.

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. *Sci Adv*. 2021 Jan 27;7(5):eabc9781.

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

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

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. doi:10.1016/j.molcel.2020.05.001.

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 $\alpha$  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<sup>+</sup> 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.

**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.

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. doi: 10.1073/pnas.1804701115. Epub 2018 Jun 18.

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. doi: 10.1016/j.cell.2018.03.001.

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. doi: 10.1016/j.celrep.2017.10.029.

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. doi: 10.18632/oncotarget.19947. eCollection 2017 Sep 12.

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. doi: 10.1038/s41598-017-05052-2

**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 DOI: 10.1126/science.aad0489

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

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**, Jacquel 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.

#### **AD-HOC JOURNAL REVIEWER:**

Cell Metabolism  
Molecular Cell \*

Cell Reports \*  
 Cancer Research  
 Nature Metabolism \*  
 Nature Communications \*  
 Cancer Discovery  
 Nature  
 Clinical Cancer Research  
 Oncogene  
 EMBO reports  
 iScience  
 Cell Death and Disease  
 Cell Chemical Biology  
 Cancers  
 The Plant Cell

\* Frequently requested as a reviewer

### **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

### **UNIVERSITY/MEDICAL SCHOOL SEMINAR INVITATIONS**

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

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

**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.

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

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

### **SCIENTIFIC CONFERENCES**

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

**Apr 2019:** 3<sup>rd</sup> edition of *Metabolism & Cancer*, Marseille, France (Invited Speaker)

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

**Jan 2018:** Keystone meeting *Tumor Metabolism*, Utah, USA (Selected speaker)

**Mar 2017:** Keystone meeting *Tumor Metabolism: Mechanisms and Targets*, Whistler, Canada (Selected Speaker)

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

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

**Sept 2014:** *Metabolism and Cancer Conference*, Nice, France (Selected Speaker)

**May 2014:** *Metabolism, Diet and Diseases, “Metabolism and Cancer”*, Washington DC, USA (Poster)

**Apr 2013:** LAM symposium, Cincinnati, OH, USA (Selected Speaker)

**Feb 2013:** Keystone meeting *Tumor Metabolism*, Denver, Colorado, USA (Selected Speaker)

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

**Jan 2008:** *World apoptosis Luxembourg* (Selected Speaker)

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

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

**Mar 2008:** *Alfediam Bruxelles* (Selected Speaker)