

McGill University, Faculty of Medicine

Curriculum Vitae for Promotions and Tenure Considerations

Date of Last Revision: April, 12, 2019

**A. IDENTIFICATION**

**Lawrence Kazak, Ph.D.**

Assistant Professor

Department of Biochemistry

Rosalind and Morris Goodman Cancer Research Centre

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**B. EDUCATION**

<b>Ph.D.</b>	University of Cambridge	Biological Sciences	2013
<b>MS.c.</b>	York University	Kinesiology and Health Science	2008
<b>B.A.</b>	York University	Kinesiology and Health Science	2005

**C. APPOINTMENTS**

Department of Biochemistry, Goodman Cancer Research Centre <b>Assistant Professor</b>	Jan 2018-present
Goodman Cancer Research Centre <b>Assistant Director</b> , Metabolic Core Facility	Jan 2018-present
Dana-Farber Cancer Institute, Harvard Medical School <b>Postdoctoral Fellow</b> , Mentor: Dr. Bruce M. Spiegelman	2013-2018

**D. SPECIAL HONORS, AWARDS, RECOGNITION**

Canada Research Chair, Mitochondrial Energetics in Health and Disease, Tier 2	2018-2023
ASCB/Merton R. Bernfield Memorial Award	2017
Overseas Research Studentship	2008-2011

**E. TEACHING****1. McGill Course**

N/A

**2. Research Trainees Supervised****E.2a Undergraduate non-course supervision**

<i>Name of Trainee</i>	<i>Department</i>	<i>Student #</i>	<i>Date(mo/yr)</i>	<i>Awards</i>
Miranda Medeiros(U1)	Biochemistry	260867198	05/19-08/19	Canderel Summer Internship
Camille Valentin(U2)	Pharmacology	260767712	05/19-08/19	N/A
Gloria Ma(U1)	Biochemistry	260851746	09/18-04/19	N/A
Ranveer Palia(U2)	Biochemistry	260725762	09/18-03/19	N/A
Alyson Jiang(U1)	Pharmacology	260774212	05/18-09/18	N/A
Natalie Constantin(U2)	Biochemistry	260666826	05/18-09/18	USRA
Sojeong Leem(U2)	Biochemistry	260687799	05/18-07/18	Canderel Summer Internship

**E.2b Undergraduate course research supervision**

N/A

**E.2c Graduate research supervision****Students graduated under my direct supervision**

<i>Name of Trainee</i>	<i>Department</i>	<i>Date(mo/yr)</i>	<i>Degree</i>	<i>Currently</i>	<i>Awards/Fellowships</i>
N/A					

**Graduate students currently under my direct supervision**

<i>Name of Trainee</i>	<i>Department</i>	<i>Date(mo/yr)</i>	<i>Degree</i>	<i>Currently</i>	<i>Awards/Fellowships</i>
Anna Roesler	Biochemistry	09/18-	MSc	Biochem, McGill	
Faiz Hussain	Biochemistry	09/18-	MSc	Biochem, McGill	
Tianxiao Yang	Biochemistry	09/19-	PhD	Biochem, McGill	
Christien Dykstra	Biochemistry	09/19-	MSc	Biochem, McGill	

**E.2d Postdoctoral research supervision****Postdoctoral fellows under my direct supervision**

<i>Name of Trainee</i>	<i>Department</i>	<i>Date(mo/yr)</i>	<i>Degree</i>	<i>Currently</i>	<i>Awards/Fellowships</i>
Janane F. Rahbani	Biochemistry	03/18-	PDF	Biochem, McGill	Canderel, 2018

**3. Invited Lectures, Talks, Presentations**

		<i>Date(mo/yr)</i>
McGill University	<i>Department of Physiology Seminar Series</i>	04/19
UBC	<i>Biochemistry and Molecular Biology Seminar Series</i>	04/19
York University	<i>Muscle Health Research Center Seminar Series</i>	04/19
Cornell University	<i>Nutrition Seminar Series</i>	03/19

Bellairs Workshop	<i>Cell and Systems Biology of Disease</i>	01/19
MUHC-RI	<i>Meakins-Christie Research Seminar Series</i>	01/19
MUHC-RI	<i>Endocrine Rounds</i>	12/18
IRCM	<i>Cardiovascular and Metabolic Diseases Seminar Series</i>	06/18
MSKCC	<i>Obesity, Cancer, and Metabolic Diseases Seminar Series</i>	05/18
ASBMB/EB	<i>New Frontiers in Substrate Metabolism</i>	04/18
ASCB EMBO	<i>Merton Bernfield Award lecture</i>	12/17
UPenn	<i>Institute for Diabetes, Obesity, and Metabolism</i>	04/16
Harvard Med School	<i>Cell Biology Seminar Series</i>	02/15
Keystone Symposia	<i>Diabetes and Metabolic Dysfunction</i>	01/15

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#### 4. Clinical Teaching

N/A

#### 5. Continued learning

Tricks and Tips, workshop on efficient teaching in biomedical sciences 05/19

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### F. OTHER CONTRIBUTIONS

#### 1. Journals

##### F.1a Ad hoc reviews

Nucleic Acids Research (7), Journal of Clinical Investigation (3), Scientific Reports (2), Nature Metabolism (1), Nature Communications (1), Biochemical Journal (1), Molecular Metabolism (1), Endocrine Reviews (1), PLOS One (1), EBioMedicine (1), Pharmaceuticals (1)

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#### 2. Grant Reviews

##### F.2a Panel Member

N/A

##### F.2b Ad hoc reviews

Czech Science Foundation	2018
<i>I reviewed a grant application at the request of the Czech Science Foundation</i>	
Breast Cancer Now/UK Breast Cancer Charity	2019
<i>I reviewed a grant application at the request of Breast Cancer Now</i>	

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### 3. Administrative Responsibilities

#### F.3a McGill - Current

Assistant Director, Metabolic Core Facility, GCRC	09/18-present
Chair, PI monthly Science Meeting, GCRC	09/18-present
Faculty representative, Graduate student Training Program Committee, GCRC	04/19-present

#### F.3b McGill - Past

Internal Studentship Evaluating Committee, GCRC	05/19
Diane and Sal Guerrero Tour Committee, GCRC	05/19
Artificial Intelligence Tour Committee, GCRC	05/19

#### F.3c Hospital - Current

N/A

#### F.3d Hospital - Past

N/A

### 4. Committees

#### F.4a Research Advisory Committee

<i>Name of Trainee</i>	<i>Supervisor</i>	<i>Department</i>	<i>Date(mo/yr)</i>	<i>Degree</i>
Marina Fukano	Morag Park	Biochemistry	05/19	MSc
Maia Al-Masri	Luke McCaffrey	Biochemistry	05/19	PhD
Samantha Garnett	David Dankort	Biology	01/19	PhD
Xianbing Zhu	Sidong Huang	Biochemistry	11/18	PhD
Zheng Fu	Sidong Huang	Biochemistry	11/18	PhD
Ipshita Nandi	William Muller	Biochemistry	09/18	MSc
George Sung	Kalle Gehring	Biochemistry	05/18; 04/19	MSc

#### F.4b Thesis defense

##### Internal Examiner

<i>Name of Trainee</i>	<i>Supervisor</i>	<i>Department</i>	<i>Date(mo/yr)</i>	<i>Type of exam</i>
Sevan Mattie	Heidi McBride	Biochemistry	01/19	PhD defense
Colin Ratcliffe	Morag Park	Biochemistry	04/18	PhD defense
Erin Coyne	Simon Wing	Biochemistry	03/18	PhD defense

#### F.4c Oral comprehensive exam

##### External Evaluator

<i>Name of Trainee</i>	<i>Supervisor</i>	<i>Department</i>	<i>Date(mo/yr)</i>	<i>Type of exam</i>
Stephanie Totten	Josie Ursini-Siegel	Biochemistry	11/18	PhD

## 5. Professional and/or Learned Societies

### F.5a Current

American Society for Biochemistry and Molecular Biology, member	12/17-present
American Society for Cell Biology, member	12/17-present

### F.5b Past

Biochemical Society, member	2008-2013
Canadian Society for Exercise Physiology, member	2005-2008

## 6. Other Professional and Scientific Contributions

### F.6a Contribution to Scientific Conferences

<b>Session Chair</b> <i>New Frontiers in Substrate Metabolism</i>	ASBMB/EB	Apr 2018
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## G. RESEARCH

### 1. Research Activities

#### G.1a Current

My research interests are focused on identifying the molecular determinants of mammalian energy metabolism, with a focus on the control of thermogenesis in brown adipose tissue. Activation of brown fat has tremendous capacity to combat obesity and obesity associated disorders, such as type 2 diabetes, hypertension and many cancers. In addition, my research is also focused on understanding cellular proteostatic mechanisms that are influenced by mitochondrial function, utilizing brown adipocytes as a model system. Finally, my lab is leveraging our expertise in cellular metabolism and applying this to non-adipose cell types that rely heavily on mitochondrial function, such as cells of the immune system.

#### G.1b Past

My past research interests have always centered on mitochondrial biology. In the past, I was involved in studying mechanisms of mitochondrial DNA replication and the role of alternative translation initiation on the trafficking of proteins to mitochondria.

### 2. Personal Support Awards

Canada Research Chair in Mitochondrial Energetics in Health and Disease, Tier 2	2018-2023
Amount: \$500,000 (CAD)	

### 3. Research Grants

#### G.3a Current

Source: **NSERC – Discovery Grant**

Program Title: Mechanisms of mitochondrial proteostasis in mammals

Role: Principal Investigator

Start Date: 04/2019

End Date: 03/2024

Amount: \$205,000 (CAD)

Source: **NSERC – Discovery Launch Supplement for Early Career Researchers**

Program Title: Mechanisms of mitochondrial proteostasis in mammals

Role: Principal Investigator

Start Date: 04/2019

End Date: 03/2020

Amount: \$12,500 (CAD)

Source: **CIHR – Project Grant (PJT 159529)**

Program Title: Physiology and mechanisms of adipocyte creatine energetics

Role: Principal Investigator

Start Date: 07/2018

End Date: 06/2023

Amount: \$833,850 (CAD)

Source: **CIHR – Project Grant (PJT 156397)**

Program Title: Investigating LKB1-mediated inflammation as a mediator of tumour progression

Role: Co-Investigator

Start Date: 07/2018

End Date: 06/2023

Amount: \$351,335 (CAD)

Source: **GCRC – New Investigator Recruitment Package**

Program Title: Mitochondrial energetics in health and disease

Role: Principal Investigator

Start Date: 01/2018

End Date: 12/2020

Source: **McGill Faculty of Medicine – New Investigator Recruitment Package**

Program Title: Mitochondrial energetics in health and disease

Role: Principal Investigator

Start Date: 01/2018

End Date: 12/2020

#### G.3b Past

Source: **NIH Pathway to Independence Award (K99/R00) (DK114528-01) - *declined***

Program Title: Creatine metabolism in obesity and diabetes

Role: Principal Investigator

Start Date: 07/2017

End Date: 06/2019

Amount: \$90,000/year (USD)

Source: **CIHR – Postdoctoral Fellowship (MFE 135539)**

Program Title: Beige adipocyte mitochondria: proteomic analysis and metabolic characterization

Role: Principal Investigator

Start Date: 07/2014

End Date: 06/2017

Amount: \$50,000/year (CDN)

Source: **Cambridge Commonwealth Trust**

Program Title: Beige adipocyte mitochondria: proteomic analysis and metabolic characterization

Role: Principal Investigator

Start Date: 10/2008

End Date: 09/2011

Amount: £10,000/year (GBP)

#### 4. Publications

##### G.4a Articles in peer reviewed journals

*Directly supervised trainees are underlined*

*§Co-first authorship*

*#Co-corresponding authorship*

1. **Kazak L<sup>#</sup>**, Rahbani JF, Samborska B, Lu GZ, Jedrychowski MP, Lajoie M, Zhang S, Ramsay LC, Dou FY, Tenen D, Chouchani ET, Dzeja P, Watson IR, Tsai L, Rosen ED, and Spiegelman BM<sup>#</sup> (2019). Ablation of adipocyte creatine transport impairs thermogenesis and causes diet-induced obesity. *Nature Metabolism*.
2. Dumesic PA, Egan DF, Gut P, Tran MT, Parisi A, Chatterjee N, Jedrychowski MP, Paschini M, **Kazak L**, Wilensky SE, Dou F, Bogoslavski D, Cartier JA, Perrimon N, Kajimura S, Parikh SM, and Spiegelman BM (2019). An Evolutionary Conserved uORF Regulates PGC1a and Oxidative Metabolism in Mice, Flies, and Bluefin Tuna. *Cell Metabolism*.
3. Chouchani ET<sup>#</sup>, **Kazak L<sup>#</sup>** and Spiegelman BM<sup>#</sup> (2019). New Advances in Adaptive Thermogenesis: UCP1 and Beyond. *Cell Metabolism*. 29(1):27-31.
4. Cluett TJ, Akman G, Reyes A, **Kazak L**, Mitchell A, Wood SR, Spinazzola A, Spelbrink JN and Holt IJ (2018). Transcript availability dictates the balance between strand-asynchronous and strand-coupled mitochondrial DNA replication. *Nucleic Acids Research*. 46(20):10771-10781.

5. Kong X, Yao T, Zhou P, **Kazak L**, Tenen D, Lyubetskaya A, Dawes BA, Tsai L, Kahn BB, Spiegelman BM, Liu T, Rosen ED (2018). Brown Adipose Tissue Controls Skeletal Muscle Function via the Secretion of Myostatin. *Cell Metabolism*. 28(4):631-643.
6. Mills EL, Pierce KA, Jedrychowski MP, Garrity R, Winther S, Vidoni S, Yoneshiro T, Spinelli JB, Lu GZ, **Kazak L**, Banks AS, Haigis MC, Kajimura S, Murphy MP, Gygi SP, Clish CB, and Chouchani ET (2018). Accumulation of systemic succinate controls activation of adipose tissue thermogenesis. *Nature*. 560(7716):102-106
7. Paulo JA, Jedrychowski MP, Chouchani ET, **Kazak L**, and Gygi SP. (2018). Multiplexed Isobaric Tag-Based Profiling of Seven Murine Tissues Following In Vivo Nicotine Treatment Using a Minimalistic Proteomics Strategy. *Proteomics*. 18(19):1-10
8. Khandekar MJ, Banks AS, Laznik-Bogoslavski D, White JP, Choi JH, **Kazak L**, Lo JC, Cohen P, Wong KK, Kamenecka TM, Griffin PR, and Spiegelman BM. (2018). Noncanonical agonist PPAR $\gamma$  ligands modulate the response to DNA damage and sensitize cancer cells to cytotoxic chemotherapy. *PNAS*. 115(3):561-566.
9. **Kazak L**<sup>#</sup>, Chouchani ET, Lu GZ, Jedrychowski MP, Bare CJ, Mina A, Kumari M, Zhang S, Vuckovic I, Laznik-Bogoslavski D, Dzeja P, Banks AS, Rosen ED, and Spiegelman BM<sup>#</sup>. (2017). Genetic depletion of adipocyte creatine metabolism inhibits diet-induced thermogenesis and drives obesity. *Cell Metabolism*. 26(4):660-671.
10. Chouchani ET, **Kazak L**, and Spiegelman BM. (2017). Mitochondrial reactive oxygen species and adipose tissue thermogenesis: bridging physiology and mechanisms. *Journal of Biological Chemistry*. 292(41):16810-16816.
11. Palmer CJ, Bruckner RJ, Paulo JA, **Kazak L**, Long JZ, Mina AI, Deng Z, LeClair KB, Hall JA, Hong S, Zushin PJH, Smith KL, Gygi SP, Hagen S, Cohen DE, Banks AS. (2017). Cdkal1, a type 2 diabetes susceptibility gene, regulates mitochondrial function in adipose tissue. *Molecular Metabolism*. 6(10):1212-1225.
12. **Kazak L**<sup>§</sup>, Chouchani ET<sup>§</sup>, Stavrovskaya IG, Lu GZ, Jedrychowski MP, Egan DF, Kumari M, Kong X, Erickson BK, Szypt J, Rosen ED, Murphy MP, Kristal BS, Gygi SP, and Spiegelman BM. (2017). UCP1 deficiency causes brown fat respiratory chain depletion and sensitizes mitochondria to calcium overload-induced dysfunction. *PNAS*. 114(30):7981-7986.
13. Bertholet AM, **Kazak L**, Chouchani ET, Bogaczynska MG, Paranjpe I, Wainwright GL, Betourne A, Kajimura S, Spiegelman BM, and Kirichok Y. (2017). Mitochondrial Patch-Clamp of Beige Adipocytes Reveals UCP1-positive and UCP1-negative Cells Both Exhibiting Futile Creatine Cycling. *Cell Metabolism*. 25(4):811-22.
14. Liyanage SU, Coyaud E, Laurent EM, Hurren R, Maclean N, Wood SR, **Kazak L**, Shamas-Din A, Holt IJ, Raught B, and Schimmer A. (2017). Characterizing the mitochondrial DNA polymerase gamma interactome by BioID identifies Ruvbl2 localizes to the mitochondria. *Mitochondrion*. 32:31-35.



15. Kumari M, Wang X, Lantier L, Lyubetskaya A, Eguchi J, Kang S, Tenen D, Roh HC, Kong X, **Kazak L**, Ahmad R, and Rosen ED. (2016). IRF3 promotes adipose inflammation and insulin resistance and represses browning. *Journal of Clinical Investigation*. 126(8):2839-54.
16. Chouchani ET<sup>§</sup>, **Kazak L**<sup>§</sup>, Jedrychowski MP, Pierce KA, Lu GZ, Laznik-Bogoslavski D, Clish CB, Robinson AJ, Gygi SP, and Spiegelman BM. (2016). Mitochondrial ROS regulate thermogenic energy expenditure and sulfenylation of UCP1. *Nature*. 532(7597):112-6.
17. **Kazak L**, Chouchani ET, Jedrychowski MP, Erickson BK, Shinoda K, Cohen P, Vetrivelan R, Lu GZ, Laznik-Bogoslavski D, Hasenfuss SC, Kajimura S, Gygi SP, and Spiegelman BM. (2015). A Creatine-Driven Substrate Cycle Enhances Energy Expenditure and Thermogenesis in Beige Fat. *Cell*. 163(3):643-55.
18. Kir S, White JP, Kleiner S, **Kazak L**, Cohen P, Baracos VE, and Spiegelman BM. (2014). Tumor-derived PTH-related protein triggers adipose tissue browning and cancer cachexia. *Nature*. 513(7516):100-4.
19. Kong X, Banks A, Liu T, **Kazak L**, Rao RR, Cohen P, Wang X, Yu S, Lo JC, Tseng YH, Cypess AM, Xue R, Kleiner S, Kang S, Spiegelman BM, and Rosen ED. (2014). IRF4 Is a Key Thermogenic Transcriptional Partner of PGC-1 $\alpha$ . *Cell*. 158(1):69-83.
20. Ye L, Wu J, Cohen P, **Kazak L**, Khandekar MJ, Jedrychowski MP, Zeng X, Gygi SP, and Spiegelman BM. (2013). Fat cells directly sense temperature to activate thermogenesis. *PNAS*. 110(30):12480-5.
21. **Kazak L**, Reyes A, He J, Wood SR, Brea-Calvo G, Holen TT, and Holt IJ. (2013). A Cryptic Targeting Signal Creates a Mitochondrial FEN1 Isoform with Tailed R-Loop Binding Properties. *PLoS One*. 8(5):e62340.
22. Reyes A, **Kazak L**, Wood SR, Yasukawa T, Jacobs HT, and Holt IJ. (2013). Mitochondrial DNA replication proceeds via a 'bootlace' mechanism involving the incorporation of processed transcripts. *Nucleic Acids Research*. 41(11):5837-50.
23. **Kazak L**<sup>#</sup>, Reyes A, Duncan A, Rorbach J, Wood SR, Brea-Calvo G, Gammage P, Robinson AJ, Minczuk M, and Holt IJ<sup>#</sup>. (2013). Alternative translation initiation augments the human mitochondrial proteome. *Nucleic Acids Research*. 41(4):2354-69.
24. **Kazak L**<sup>#</sup>, Reyes A<sup>#</sup>, and Holt IJ<sup>#</sup>. (2012). Minimizing the damage: repair pathways keep mtDNA intact. *Nature Reviews Molecular Cell Biology*. 13(10):659-71.
25. He J, Cooper HM, Reyes A, Di Re M, **Kazak L**, Wood SR, Mao CC, Fearnley IM, Walker JE, and Holt IJ. (2012). Human C4orf14 interacts with the mitochondrial nucleoid and is involved in the biogenesis of the small mitochondrial ribosomal subunit. *Nucleic Acids Research*. 40(13):6097-108.
26. Reyes A, He J, Mao CC, Bailey LJ, Di Re M, Sembongi H, **Kazak L**, Dzionek K, Holmes J.B., Cluett TJ, Harbour ME, Fearnley IM, Crouch RJ, Conti MA, Adelstein RS, Walker JE, and Holt IJ.

(2011). Actin and myosin contribute to mitochondrial DNA maintenance. *Nucleic Acids Research*. 39(12):5098-108.

27. Vainshtein A, **Kazak L**, and Hood DA. (2011). Effects of endurance training on apoptotic susceptibility in striated muscle. *Journal of Applied Physiology*. 110(6):1638-45.
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#### **G.4b Technical reports**

N/A

#### **G.4c Book chapters**

1. **Kazak L**. (2017). Bioenergetic Analyses in Adipose Tissue. In: J. Wu (Ed.). *Thermogenic Fat: Methods Molecular Biology*. 1566:125-134. Springer Nature.
2. Holt IJ, **Kazak L**, Reyes A, Wood SR (2016). Analysis of Replicating Mitochondrial DNA by In Organello Labeling and Two-Dimensional Agarose Gel Electrophoresis. In: M. McKenzie (Ed.) *Mitochondrial DNA: Methods in Molecular Biology* (Clifton, N.J.). 1351:95-113. Springer New York.
3. Saleem A, **Kazak L**, O’Leary MO, and Hood DA (2011). Cell death regulation in muscle. In: J.C. Reed and D. Green (Eds.). *Apoptosis: Physiology and Pathology*. Cambridge University Press.
4. Joseph AM, Ljubicic V, Menzies K, **Kazak L**, Uguccioni G, and Hood DA (2009). Mitochondrial biogenesis in health and disease-influence of stress stimuli. In: J Magalhaes and A. Ascensao (Eds.). *Muscle Plasticity: Advances in Physiological and Biochemical Research*. Kerala: The Research Signpost/Transworld Research Network. 151-171.

#### **G.4d Abstracts and conference presentations**

Keystone Symposia	Obesity and Adipose Tissue Biology	poster	2019
Keystone Symposia	Bioenergetics and Metabolic Disease	poster	2018
Keystone Symposia	Obesity and Adipose Tissue Biology	poster	2016
Keystone Symposia	Beige and Brown Fat	poster	2015
Keystone Symposia	Diabetes and Metabolic Dysfunction	poster	2015
Keystone Symposia	Mitochondria, Metabolism, and Heart Failure	poster	2015

#### **G.4e Others, including non-refereed publications**

N/A