

Heather Melichar

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Education

- 1995 -1999 B.S., Biology, Boston College, Chestnut Hill, MA (Tom Seyfried, Boston College, Arthur Pardee, Dana-Farber Cancer Institute)
- 2000 - 2006 Ph.D., Immunology, University of Massachusetts Medical School, Worcester, MA (Joonsoo Kang)
- 2007 - 2013 Post-doctoral, University of California, Berkeley, CA (Ellen Robey)

Other experience

- 1999 - 2000 Research Assistant / Microinjectionist, Emory University, Atlanta, GA

Academic employment

- 2014 - Professeure sous octroi agrégée (Associate Professor) (06/2019 -)
 Professeure sous octroi adjointe (Assistant Professor) (07/2014 - 05/2019)
 Professeure-chercheure adjointe (Research Assistant Professor) (01/2014 - 06/2014)
 Centre de recherche - Hôpital Maisonneuve Rosemont
 Département de médecine, Université de Montréal

Acknowledgements

- 2002/09 - 2003/09 NIH doctoral training grant
- 2006/05 International gamma-delta T cell Conference Travel Award
- 2007/10 - 2009/12 California Institute of Regenerative Medicine (CIRM) post-doctoral fellowship
- 2011/05 AAI Trainee Abstract Award
- 2012/05 AAI Trainee Abstract Award
- 2013/01 - 2013/10 California Institute of Regenerative Medicine (CIRM) post-doctoral fellowship
- 2014/07 - 2018/06 Chercheur boursier - Junior 1 - FRQS, salary award
- 2015/07 - 2020/06 CIHR New Investigator Award
- 2017/05 AAI Early Career Faculty Travel Grant
- 2019/04 CSI Early Career Faculty Travel Grant
- 2019/05 EMBO Early Career Faculty Travel Grant
- 2020/07 – 2022/06 Chercheur boursier – Junior 2 – FRQS, salary award

Professional service (selected)

- 2015, 2016, 2020 Scientific officer, 3x Review Panel, Innovation grants, Canadian Cancer Society
- 2015 - 2017 Member, 3x Post-doctoral fellowship committee, Fonds de recherche du Québec-Santé
- 2016 Co-chair, Tumor Immunology, Immunotherapy, and Vaccines workshop, Canadian Society of Immunology, Annual Meeting
- 2016 - Treasurer, Organizing committee, Meetings d'Immunologie Montréal
- 2016 - 2020 Member, 7x Review Panel, Project grants, Canadian Institutes of Health Research
- 2016 - 2020 Member, 5x Review Panel, New Investigator grants, The Hospital for Sick Children

2018	Chair, major symposium: Conventional and Unconventional T Cell Development: Fate Choices & Spatial Factors, Canadian Society of Immunology, Annual Meeting, London, ON, Canada
2019	New Frontiers in Research Fund - Exploration competition, LOI review committee
2019 -	Elected member, Canadian Society for Immunology governing council
2020	Member, Review Panel, Operating grants, Cancer Research Society
2020	External reviewer, New Frontiers in Research Fund

Student supervision (since 2014)

Undergraduate interns

2014/05 - 2014/08	Carole Arlette Bonkougou
2014/09 - 2015/05	Desiré Akaba Omgba
2015/05 - 2015/07	Fatoumata Barry
2016/05 - 2016/08	Milad Ameer
2016/05 - 2016/08	Lucas Perus (CR-HMR fellowship)
2017/01 - 2017/04	Johanna Manga
2017/05 - 2017/08	Bernice Pierre
2018/05 - 2018/08	Maria Galipeau (Diabète Québec fellowshsip)
2018/05 - 2018/08	Tu-Quan Han
2019/05 – 2019/08	Louis-Olivier Roy
2019/06 - 2019/08	Noemie Gervais

MSc

2015/01 - 2016/09	Mengqi Dong (<i>direct passage to PhD / passage accéléré au doctorat</i>)
2016/05 - 2018/05	Carole Bonkougou (UdeM fellowship)
2020/07 -	Ève Mallet Gauthier

PhD

2016/09 -	Mengqi Dong (UdeM&FRQS fellowships)
2020/09 -	Stefanie Valbon Fernandes Garcia (HMR fellowship)

Post-doctoral

2015/08 - 2018/12	Charles-Étienne Lebert-Ghali (Cole Foundation fellowship)
2015/12 -	Aditi Sood (Cole Foundation fellowship)
2016/06 - 2020/06	Marie-Ève Lebel (FRQS&L'Oreal Women in Science fellowships)
2016/08 -	Mathieu Neault (FRQS&Cole Foundation fellowships) co-supervised by Mallette
2019/01 -	Marion Dubuissez (HMR Foundation fellowship), co-supervised by Mallette
2020/11 -	Sébastien This, co-supervised by Costantino

Publications

* indicates equal contribution

trainees under my supervision are underlined

staff under my supervision are *italicized*

indicates co-corresponding authors

Peer-reviewed publications

1. **Melichar, H.**, Bosch, I., Molnar, G.M., Huang, L., and Pardee, A.B. (2000) Detection of eukaryotic cDNA in differential display is enhanced by the addition of E. coli RNA. *Biotechniques* 28, 76-82.
2. Bosch, I., **Melichar, H.**, and Pardee, A.B. (2000) Identification of differentially expressed genes from limited amounts of RNA. *Nucleic Acids Research*, 28, E27.
3. Bosch, I., Xhaja, K., Estevez, L., Raines, G., **Melichar, H.**, Warke, R.V. Fournier, M.V., Ennis, F.A., and Rothman, A.L. (2002) Increased production of interleukin-8 in primary human monocytes and in

human epithelial and endothelial cell lines after dengue virus challenge. *Journal of Virology*, 76, 5588-5597.

4. **Melichar, H.** and Kang, J. (2007) Intertwined morphogen signal inputs in $\gamma\delta$ versus $\alpha\beta$ T cell differentiation. *Immunological Reviews*, 215, 32-45.
5. **Melichar, H.J.**, Narayan, K., Der, S., Hiraoka, Y., Gardiol, N., Jeannet, G., Held, W., Chambers, C., and Kang, J. (2007) Regulation of $\gamma\delta$ versus $\alpha\beta$ T lymphocyte differentiation by the transcription factor Sox13. *Science*, 315, 230-233.
6. **Melichar, H.J.***, Li, O.* , Herzmark, P.* , Padmanabhan, R.K., Oliaro, J., Ludford-Menting, M.J., Bouso, P., Russell, S.M., Roysam., B., and Robey, E.A. (2011) Quantifying subcellular distribution of fluorescent fusion proteins in cells migrating within tissues. *Immunology & Cell Biology*, 89, 549-557.
7. **Melichar, H.***, Li, O.* , Ross, J., Haber, H., Cado, D., Nolla, H., Robey, E.A., and Winoto, A. (2011) Comparative study of hematopoietic differentiation between human embryonic stem cell lines. *PLoS One*, 6, e19854.
8. Malhotra, N.* , Narayan, K.* , Cho, O., Sylvia, K.E., Yin, C., **Melichar, H.**, Lefebvre, V., Berg, L.J., and Kang, J.; The Immunological Genome Project Consortium. (2013) A High Mobility Group box transcription factor network programs innate IL-17 production. *Immunity*, 38, 681-693.
9. Halkias, J.* , **Melichar, H.J.***, Taylor, K.T., Ross, J.O., Yen, B., Cooper, S.B., Winoto, A., and Robey, E.A. (2013) Opposing chemokine gradients control human thymocyte migration in situ. *Journal of Clinical Investigation*, 123, 2131-2142.
10. **Melichar, H.J.***, Ross, J.O.* , Herzmark, P., Hogquist, K.A., and Robey, E.A. (2013) Distinct temporal patterns of T cell receptor signaling during positive versus negative selection in situ. *Science Signaling*, 6, ra92.
11. Halkias, J., **Melichar, H.J.**, Taylor, K.T., Robey, E.A. (2014) Tracking migration during human T cell development. *Cellular and Molecular Life Sciences*, 71, 3101-3117.
12. Ross, J.O.* , **Melichar, H.J.***, Au-Yeung, B.B., Herzmark, P., Weiss, A., Robey, E.A. (2014) Two distinct phases in the positive selection of CD8⁺ T cells distinguished by intrathymic migration and TCR signaling patterns. *Proceedings of the National Academy of Sciences*, 111, E2550-2558.
13. Au-Yeung, B.B.* , **Melichar, H.J.***, Ross, J.O., Cheng, D.A., Zhang, C., Shokat, K.M., Robey, E.A., and Weiss, A. (2014) Quantitative and Temporal Requirements Revealed for Zap-70 catalytic activity during T cell development. *Nature Immunology*, 15, 687-694.
14. Han, S.J., **Melichar, H.J.**, Coombes, J.L., Chan, S.W., Barton, G.M., and Robey, E.A. (2014) Internalization and TLR-dependent type I interferon production by monocytes in response to *Toxoplasma gondii*. *Immunology & Cell Biology*, 92, 872-881.
15. **Melichar, H.J.***, Ross, J.O.* , Taylor, K.T. Robey, E.A. (2015) Stable interactions and sustained T cell receptor signaling typify thymocyte-thymocyte interactions that support negative selection. *The Journal of Immunology*. 194,1057-6101.
16. Halkias, J., Yen, B., Reinhartz, O., Taylor, K.T., Winoto, A., Robey, E.A., and **Melichar, H.J.** (2015) Conserved and divergent aspects of human T cell development and migration in humanized mice. *Immunology & Cell Biology*, 93, 716-726.
17. Pham, K., Shimoni, R., Charnley, M., Ludford-Menting, M., Hawkins, E.D., Ramsbottom, K., Oliaro, J., Izon, D., Ting, S.B., Reynolds, J., Lythe, G., Molina-Paris, C., **Melichar, H.**, Robey, E., Humbert, P.O., Gu, M., and Russell, S.M. (2015) Asymmetric cell division during T cell development controls downstream fate. *The Journal of Cell Biology*, 210, 933-950.
18. Sood, A.*, Dong, M.*, and **Melichar, H.J.** (2016) Preparation and applications of organotypic thymic slice cultures. *Journal of Visualized Experiments*, 114, e54355.

19. Mathieu, M., Odagiu, L., Gaudot, L., Daudelin, J-F., **Melichar, H.J.**, Lapointe, R., and Labrecque, N. (2017) Inflammation enhances the vaccination potential of CD40 activated B cells. *European Journal of Immunology*, 47, 269-279.
20. Lebert-Ghali, C-È., Thompson, A., **Melichar, H.J.**, and Bijl, J.J. (2017) Targeted deletion of the Hoxa cluster affects B lymphopoiesis through depletion of early lymphoid progenitors. *Experimental Hematology*, 50, 84-89.e3.
21. Dong, M., Artusa, P., Kelly, S.A., *Fournier, M.*, Baldwin, T.A., Mandl, J.N., and **Melichar, H.J.** (2017) Alternations in the thymic selection threshold skew the self-reactivity of the T cell receptor repertoire in neonates. *The Journal of Immunology*, 199, 965-973.
22. Spidale, N.A.*, Sylvia, K.*, Narayan, K., Miu, B., Frascoli, M., **Melichar, H.J.**, Zhihao, W., Kisielow, J., Palin, A., Serwold, T., Love, P., Kobayashi, M., Yoshimoto, M., Jain, N., and Kang, J. (2018) Interleukin-17 producing $\gamma\delta$ T cells originate from SOX13+ progenitors that are independent of $\gamma\delta$ TCR signaling. *Immunity*, 49, 857-872.
23. Apavaloaei, A., Brochu, S., Dong, M., Rouette, A., Hardy, M-P., Villafano, G., Murata, S., **Melichar, H.**, and Perreault, C. (2019) PSMB11 orchestrates the development of CD4 and CD8 thymocytes via regulation of gene expression in cortical thymic epithelial cells. *The Journal of Immunology*, 202, 966-978.
24. Sood, A., Lebel, M-È., *Fournier, M.*, Rogers, D., Mandl, J.N., **Melichar, H.J.** (2019) Differential interferon-gamma production potential among naïve CD4⁺ T cells exists prior to antigen encounter. *Immunology & Cell Biology*, 97, 931-940.
25. Viallard, C., Audiger, C., Akla, N., Legault-Navarette, I., **Melichar, H.**, Costantino, S., Lesage, S., and Larrivée, B. (2020) BMP9 signaling promotes the normalization of tumor blood vessels. *Oncogene*, 39: 2996-3014.
26. Collin, R., Lombard-Vadnais, F., Hillhouse, E.E., Lebel, M-È., Chabot-Roy, G., **Melichar, H.J.**, Lesage, S. (2020) MHC-independent thymic selection of immunomodulatory CD4 and CD8 coreceptor negative $\alpha\beta$ T cells. *The Journal of Immunology*, 205: 133-142.
27. Lebel, M-È., Coutelier, M., Galipeau, M., Kleinman, C.L., Moon, J.J. **Melichar, H.J.** (2020) Differential expression of tissue restricted antigens among mTEC is associated with distinct autoreactive T cell fates. *Nature Communications*, 11: 3734.

Manuscripts submitted/in revision

28. Boulet, S., Odagiu, L., Dong, M., Lebel, M-È., Daudelin, J-F., **Melichar, H.J.**, Labrecque, N. NR4A3 mediates thymic negative selection. (*The Journal of Immunology*, in revision)
29. Sood, A., Lebel, M-È., Dong, M., *Fournier, M.*, Vobecky, S.J., Haddad, É., Delisle, J-S., Mandl, J.N., Vriskoop, N.#, **Melichar, H.J.#** CD5 levels define functionally heterogeneous populations of naïve human CD4⁺ T cells. (*European Journal of Immunology*, in revision)
30. Dong, M., Audiger, C., Adegoke, A., Valbon, S.F., Lebel, M-È., Anderson, C., **Melichar, H.J.#**, Lesage, S.# CD5 levels reveal distinct basal TCR signals in T cells from NOD mice. (*Immunology & Cell Biology*, in revision)
31. Janelle, V., Neault, M., Lebel, M-È., De Sousa, D., Boulet, S., Durrieu, L., Carli, C., Labrecque, N., **Melichar, H.J.**, Mallette, F.A., Delisle, J-S. Caspase-8 limits DNA damage and senescence-associated features in human T cells. (submitted)
32. Dong, M.*, Mallet Gauthier, È.*, *Fournier, M.*, **Melichar, H.J.#** Developing the right tools for the job: Thymopoiesis in the fetus, neonate, and adult. (invited review, submitted)

Book Chapters

1. Bosch, I., Warke, R., Fournier, M., Magee, D., and **Melichar, H.** (2004) Applications of differential display in infectious diseases. In: Weissensteiner, T., Griffin, H., and Griffin, A., eds. PCR technology: current innovations. Boca Raton, FL; London: CRC Press.
2. Dzhagalov, I.L., **Melichar, H.J.**, Ross, J.O., Herzmark, P., and Robey, E.A. (2012) Two-photon imaging of the immune system. *Current Protocols in Cytometry*, 60, 12.26.1-12.26.20.
3. Ross, J.O., **Melichar, H.J.**, Halkias, J., and Robey, E.A. (2016) Studying T cell development in thymic slices. *Methods in Molecular Biology: T cell development*, 1323, 131-140.
4. Labrecque, N.#, Dong, M.*, Sood, A.*, and **Melichar, H.J.** (2018) *In situ* analysis of T cell receptor signals during positive selection. In: Soboloff, J. and Kappes, D.J. eds. Signaling Mechanisms Regulating T Cell Diversity and Function. Boca Raton, FL; London: CRC Press.
5. *Fournier, M.**, Dong, M.*, **Melichar, H.J.#** (2020) Investigating T cell receptor signalling dynamics *in situ* by two-photon microscopy of thymocytes expressing genetic reporters in low-density chimeras. *Methods in Molecular Biology: T-Cell Receptor Signaling. Methods in Molecular Biology: T-Cell Receptor Signaling*. 2111, 221-238.

Invited talks and conference presentations (last 5 years)

14. Canadian Society of Immunology Annual Meeting, Québec, Qc, 2014
“A T cell receptor signal threshold determines positive selection”
15. INRS-Institut Armand-Frappier, Laval, Qc, 2014
“Visualizing the dynamics of T cell receptor signaling throughout thymocyte development”
16. Université de Montréal, Département de microbiologie, infectionologie, et immunologie, Montréal, Qc, 2014
“Visualizing the dynamics of T cell receptor signaling throughout thymocyte development”
17. Scientific Retreat - CR-Hôpital Maisonneuve-Rosemont, Mont Gabriel, Qc, 2014
“Visualizing the dynamics of T cell receptor signaling throughout thymocyte development”
18. Cole Foundation-NEW IDEAS from a NEW GENERATION of LEUKEMIA/LYMPHOMA Researchers, Montréal, Qc, 2015
“T cell suppression by a novel co-stimulatory molecule interaction with implications in the treatment of GVHD”
19. Cole Foundation-Research Celebration Day, Montréal, Qc, 2015
“T cell suppression by a novel co-stimulatory molecule interaction with implications in the treatment of GVHD”
20. Meetings d'Immunologie Montréal, McGill University, Montréal, Qc, 2015
“Dynamic T cell receptor signaling during thymic selection: cause and effect”
21. Université de Sherbrooke, Département de pédiatrie, Division d'immunologie, Sherbrooke, Qc, 2015
“Dynamic T cell receptor signaling during thymic selection: cause and effect”
22. Cole Foundation-Leukemia Summit, Ste-Adèle, Qc, 2015
“T cell suppression by a novel co-stimulatory molecule interaction with implications in the treatment of GVHD”
23. University of Alberta, Alberta Transplant Institute, Edmonton, Ab, 2015
“Dynamic T cell receptor signaling during thymic selection: cause and effect”
24. McGill University, Department of Microbiology and Immunology, Montréal, Qc, 2016
“Revisiting the affinity model: the spatio-temporal dynamics of thymic selection”

25. Federation of Clinical Immunology Societies - Centre of Excellence in Translational Immunology Annual Symposium, Montréal, Qc, 2017
"Functional heterogeneity within the naive T cell population"
26. CR-CHU Ste-Justine, Montréal, Qc, 2018
"Self-reactive T cells: many shades of gray"
27. The Research Institute of the McGill University Health Centre, Montréal, Infectious Diseases and Immunity in Global Health program, Montréal, Qc, 2018
"Self-reactive T cells: many shades of gray"
28. The University of Texas at Austin, Department of Molecular Biosciences Seminar Series, Austin, TX, 2018
"Self-reactive T cells: many shades of gray"
29. Banff International Research Station / Casa Matematica Oaxaca : Quantitative analysis of immune cell migration and spatial processes in health and disease, Oaxaca, Mexico 2018
"Revisiting the affinity model: the spatio-temporal dynamics of thymic selection"
30. Centre International de Recherche en Infectiologie, INSERM U1111 - CNRS UMR5308, Université Lyon, Lyon, France, 2018
"Self-reactive T cells: many shades of gray"
31. 5^{ème} Annual symposium, Meetings d'Immunologie Montréal : Spatial processes in adaptive immunity, Montréal, Qc, Canada, 2018
"Self-reactive T cells: many shades of gray"
32. Genentech, Inc., Cancer Immunology, South San Francisco, CA, 2019
"Self-reactive T cells: many shades of gray"
33. EMBO Workshop, ThymE: T cell and Thymus Biology, Weizmann Institute of Science, Rehovot, Israel, 2019
"Tissue restricted antigen expression by medullary thymic epithelial cell subsets induces distinct T cell fates"
34. Université de Montréal, Département de pharmacologie et physiologie, Montréal, Qc, Canada, 2020
"Self-reactive T cells : many shades of gray"
35. University of Ottawa, Advances in Biomedical Research seminar series, Department of Biochemistry, Immunology and Microbiology and the Departments of Cellular & Molecular Medicine, Ottawa, ON, Canada – VIRTUAL, 2020
"Cellular and molecular brakes on T cell function"

Current funding

2015-2020

The Canadian Institutes of Health Research (CIHR)

"Determining cause and effect: dynamic T cell receptor signaling during thymic selection"

Operating grant

PI

2018-2021

Canadian Cancer Society Research Institute – Division du Québec and the Cole Foundation (Mont Gabriel Summit)

"Identification of therapeutic targets for pediatric acute megakaryoblastic leukemia"

Operating grant

Co-I with Dr Frédérick Antoine Mallette (PI), co-applicants: Drs Elliot Drobetsky, Anne-Claude Gingras, Jean-Sébastien Delisle, and Sidong Huang

2018-2023

Canadian Institutes of Health Research (CIHR)

“Identification of therapeutic targets for pediatric acute megakaryoblastic leukemia”

Operating grant

PI with Dr Frédérick Antoine Mallette (PI) and co-applicants Drs Elliot Drobetsky, Anne-Claude Gingras, and Jean-Sébastien Delisle

2018-2021

Fonds de recherche du Québec - Nature et technologies (FRQNT)

“Identification and isolation of single cells to understand asymmetric cell division”

Operating (team) grant

Co-applicant with Drs Santiago Costantino (PI) and Christos Boutopoulos

2018-2020

Cancer Research Society

“Aberrant expression of terminal deoxynucleotidyl transferase as a novel biomarker for the efficacy of checkpoint blockade immunotherapy”

Operating grant

PI with co-applicants Drs Elliot Drobetsky, Judith Mandl, Virginie Royal

2019-2024

NSERC

“Intrinsic and environmental influences on thymocyte migration signatures”

Operating grant

PI

2019-2020

Diabète Québec

“Le rôle de la tolérance des lymphocytes T dans le développement du diabète”

Operating grant

PI

2019-2021

Cancer Research Society

“The anti-tumour potential of targeting an ‘orphan’ tumour necrosis factor receptor”

Operating grant

PI

2020-2025

Canadian Institutes of Health Research (CIHR)

“Regulation of thymic selection thresholds and their role in establishing T cell function”

Operating grant

PI with Judith Mandl (PI)