

**Darren Freed**

MD PhD FRCSC

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**Professional Overview:**

Dr. Darren Freed is a native Albertan, recently relocated back to Edmonton from Winnipeg. He is a cardiac surgeon clinician-scientist with an interest in heart and lung failure and novel techniques to treat these conditions. His primary clinical interests are in cardiothoracic transplantation and mechanical circulatory assistance as well as less invasive cardiac surgery. His primary research interests are in ex vivo organ perfusion, heart transplantation, mechanical circulatory support and the biological basis of myocardial fibrosis. He obtained his MD from the University of Alberta in 1998 and completed his cardiac surgical training at the University of Manitoba where he also obtained a PhD in Physiology in 2004. In 2007 he completed a Clinical Fellowship in Cardiothoracic Transplantation and Ventricular Assist Devices at Papworth Hospital in Cambridge, United Kingdom. He is currently an Associate Professor, Division of Cardiac Surgery, Department of Surgery, with cross appointments in the Departments of Physiology and Biomedical Engineering. He is the Director of Research for the Alberta Transplant Institute.

**Industry Relationships:**

- XVIVO Perfusion

- Maquet
- Sorin
- Medtronic

## Current Research Interests:

- Ex vivo organ perfusion for transplantation
- Heart and lung transplantation
- Ventricular Assist Devices
- Myocardial wound healing and fibrosis
- Stem cell biology
- MicroRNA

## Publications:

1. Sakamuri SS, Takawale A, Basu R, Fedak PW, **Freed D**, Sergi C, Oudit GY, Kassiriz. Differential impact of mechanical unloading on structural and non-structural components of the extracellular matrix in advanced human heart failure. *TranslRes*. 2016 Feb 23. pii: S1931-5244(16)00060-8. doi: 10.1016/j.trsl.2016.02.006. [Epub ahead of print] PubMed PMID: 26963743.
2. Lee TW, Kowalski S, Falk K, Maguire D, **Freed DH**, HayGlass KT. High Spinal Anesthesia Enhances Anti-Inflammatory Responses in Patients Undergoing Coronary Artery Bypass Graft Surgery and Aortic Valve Replacement: Randomized Pilot Study. *PLoS One*. 2016 Mar 1;11(3):e0149942. doi: 10.1371/journal.pone.0149942. eCollection 2016. PubMed PMID: 26930568; PubMed Central PMCID: PMC4773142.
3. Wang J, Xiang B, Deng J, **Freed DH**, Arora RC, Tian G. Inhibition of Viability, Proliferation, Cytokines Secretion, Surface Antigen Expression, and Adipogenic and Osteogenic Differentiation of Adipose-Derived Stem Cells by Seven-Day Exposure to 0.5 T Static Magnetic Fields. *Stem Cells Int*. 2016;2016:7168175. doi:10.1155/2016/7168175. Epub 2016 Jan 6. PubMed PMID: 26880984; PubMed Central PMCID: PMC4736570.
4. Nagendran J, Moore MD, Norris CM, Khani-Hanjani A, Graham M, **Freed DH**, Nagendran J. The varying effects of obesity and morbid obesity on outcome following cardiac transplantation. *Int J Obes (Lond)*. 2016 Apr;40(4):721-4. doi: 10.1038/ijo.2016.20. Epub 2016 Feb 8. PubMed PMID: 26853917.
5. Senaratne JM, Norris CM, Graham MM, Galbraith D, Nagendran J, **Freed DH**, Afilalo J, Van Diepen S; APPROACH Investigators. Clinical and angiographic outcomes associated with surgical revascularization of angiographically borderline 50-69% coronary artery stenoses†. *Eur J Cardiothorac Surg*. 2016 Jan 29. pii: ezw005. [Epub ahead of print] PubMed PMID: 26825107.
6. White CW, Ambrose E, Müller A, Li Y, Le H, Thliveris J, Arora RC, Lee TW, Dixon IM, Tian G, Nagendran J, Hryshko LV, **Freed DH**. Avoidance of Profound Hypothermia During Initial Reperfusion Improves the Functional Recovery of Hearts Donated After Circulatory Death. *Am J Transplant*. 2016 Mar;16(3):773-82. doi:10.1111/ajt.13574. Epub 2016 Jan 18. PubMed PMID: 26780159.
7. Müller AL, **Freed DH**. Basic and Clinical Observations of Mevalonate Depletion on the Mevalonate Signalling Pathway. *Curr Mol Pharmacol*. 2016 Jan 12. [Epub ahead of print] PubMed PMID: 26758946.
8. White CW, Lilloco R, Sandha J, Hasanally D, Wang F, Ambrose E, Müller A, Rachid O, Li Y, Xiang B, Le H, Messer S, Ali A, Large SR, Lee TW, Dixon IM, Lakowski TM, Simons K, Arora RC, Tian G, Nagendran J, Hryshko LV, **Freed DH**. Physiologic Changes in the Heart Following Cessation of Mechanical Ventilation in a Porcine Model of Donation After Circulatory Death: Implications for Cardiac Transplantation. *Am J Transplant*. 2016

Mar;16(3):783-93. doi: 10.1111/ajt.13543. Epub 2015 Dec 11. PubMed PMID: 26663659.

9. Manji RA, Arora RC, Singal RK, Hiebert B, Moon MC, **Freed DH**, Menkis AH. Long Term Outcome and Predictors of Non-Institutionalized Survival after Prolonged ICU Stay Post Cardiac Surgery. *In press, Ann Thorac Surg*.
10. Bordun KA, Premecz S, daSilva M, Mandal S, Goyal V, Glavinovic T, Cheung M, Cheung D, White C, Chaudhary R, **Freed D**, Villarraga H, Herrmann J, Kohli M, Ravandi A, Thliveris J, Pitz M, Singal P, Mulvagh S, Jassal D. The utility of cardiac biomarkers and echocardiography for the early detection of bevacizumab and sunitinib mediated cardiotoxicity. *In press, Am J Physiol – Heart and Circulatory Physiology*.
11. Luc JG, Zhao, J, Michelakis ED, **Freed DH**, Nagendran J. Gender specific Influences on Effector T-Cell function and proliferation: Hormonal Targeting to Modulate Cellular Rejection in Transplantation. *In press, Transplant Proc*.
12. White CW, Li Y, Ambrose E, Muller A, Le H, Hiebert B, Arora RC, Lee TW, Tian G, Nagendran J, Hryshko LV, **Freed DH**. Assessment of donor heart viability during *ex vivo* heart perfusion. *In press, Can J Physiol Pharmacol*.
13. Dietz B, Alexander M, Elhami E, Xiang B, Deng J, Wang F, Chi C, Goertzen AL, Mzengeza S, **Freed D**, Arora RC, Tian G. New Software for Multimodal Image Registration with Application in Cell Tracking Studies. *In press, J Stem Cell Res Ther*.
14. Bednarczyk JM, Reddy S, White CW, **Freed DH**, Bell D, Ahmed SZ, Kumar A, Light B. Extracorporeal membrane oxygenation facilitates survival in blastomycosis related acute respiratory distress syndrome. *In press, Can J Anesth*.
15. Natarajan K, Tian C, Xiang B, Chi C, Deng J, Zhang R, **Freed DH**, Arora RC, Tian G, Lin F. Selection of chemotactic adipose-derived stem cells using microfluidic gradient generator. *In press, RSC Advances*.
16. Freed DH, White CW. Donor heart preservation: straight up, or on the rocks? *Lancet*. 2015 Apr 14 [Epub ahead of print].
17. Wang J, Xiang B, Lin H-Y, Liu H-Y, **Freed D**, Arora RC, Tian G. Collateral circulation determines characteristic profiles of contrast-enhanced MRI in the infarcted myocardium. *Acta Pharmacol Sinica*. 2015 Apr;36(4):463-472.
18. Wang J, Xiang B, Lin H-Y, Liu H, **Freed D**, Arora RC, Tian G. Differential MR delayed enhancement patterns of chronic myocardial infarction between extracellular and intravascular contrast media. *PLoS One*. 2015 Mar 27;10(3):e0121326.
19. Ghavami S, Cunnington RH, Yeganeh B, Bathe K, Gupta S, **Freed DH\***, Halayko AJ\*, Klonisch T\*, Dixon IMC\*. Autophagy is a regulator of TGF- $\beta$  induced fibrogenesis in primary human atrial myofibroblasts. *Cell Death Dis*. 2015 Mar 19;6:e1696. \*these authors share senior authorship.
20. Bozso S, Sidhu S, Garg M, **Freed DH**, Nagendran J. Canada's Longest Experience with Extracorporeal Membrane Oxygenation as a Bridge to Lung Transplantation – A Case Report. *Transplant Proc*. 2015 Jan-Feb;47(1):189-9.
21. Luc JGY, Bozso S, **Freed DH**, Nagendran J. Successful Repair of DCD Lungs with Large Pulmonary Embolus Using the Lung OCS System for Ex-Vivo Thrombolysis and Subsequent Clinical Transplantation. *Transplantation*. 2015 Jan 15;99(1):e1-2.
22. Chi C, Wang F, Xiang B, Deng J, Liu S, Lin H-Y, Natarajan K, Lin F, **Freed DH**, Arora RC, Liu H, Tian G. Adipose-Derived Stem Cells from both Visceral and Subcutaneous Fat Deposits Significantly Improve Contractile Function of Infarcted Rat Hearts. *Cell Transplant*. 2015 Jan 5 [Epub ahead of print].

23. Li Y, Muller AL, Ngo MA, Sran KK, Arora RC, Kirshenbaum LA, **Freed DH**. Statins Impair Survival of Primary Human Mesenchymal Progenitor Cells via Mevalonate Depletion, NF- $\kappa$ B Signaling and Bnip3. *J Cardiovasc Transl Med*. 2014 Dec 30. [Epub ahead of print].
24. Bashir J, Legare JF, **Freed DH**, Cheung A, Rao V, Toma M. Multi-center Canadian Experience with the HeartWare Ventricular Assist Device. *Can J Cardiol*. 2014 Dec;30(12):1662-7.
25. Sytnik P, White CW, Nates W, Lytwyn M, Strumpher J, Arora RC, **Freed DH**. Aorto-right atrial fistula complicating a type A dissection: case report and review of the literature. *J Card Surg*. 2014 Dec 29.
26. Bozso SJ, Vasanthan V, **Freed DH**, Nagendran J. Lung Transplantation from Donors after Circulatory Death using Portable Ex-Vivo Lung Perfusion. *Can Resp J*. 2014 Nov 6. [Epub ahead of print].
27. Golian M, **Freed DH**, Ravandi A. Successful resuscitation with ECMO in the setting of persistent ventricular fibrillation. *BMC Research Notes*. 2014 Nov 4;7:782.
28. Bednarczyk JM, Ducas RA, White CW, Golian M, Nepomuceno R, Bueddefeld D, Manji RA, Hussain F, **Freed DH**. Extracorporeal Membrane Oxygenation facilitates survival in refractory in-hospital cardiac arrest and cardiogenic shock: a Canadian perspective. *Resuscitation*. 2014 Oct 17;85(12):1713-19.
29. Bozso SJ, **Freed DH**, Nagendran J. Successful Transplantation of Extended Criteria Lungs After Prolonged Ex-Vivo Lung Perfusion Performed on a Portable Device. *Transpl Int*. 2014 Oct 5.
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31. Karlstedt E, Jassal DS, Kirkpatrick IDC, **Freed DH**, Seifer CM. Multimodality cardiac imaging of infective endocarditis. *J Cardiovasc Med*. 2014 Jul 10. [Epub ahead of print].
32. Menard CE, Durston M, Zhrebetskaya E, Smith DR, **Freed DH**, Tian G, Fernyhough P, Arora RC. Temporal Dystrophic Remodeling within the Intrinsic Cardiac Nervous System of the Streptozotocin-Induced Diabetic Rat Model. *Acta Neuropath Comm*. 2014 Jun 4;2:60.
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34. Liu S, Horne D, **Freed DH**, Sookhoo S, Strzelczyk J, Ravandi A, Jassal DS. Multimodality Imaging of a Cardiac Pheochromocytoma. *J Am Coll Cardiol*. 2014 Jun 17;63(23):e189.
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36. Wang J, Xiang B, Lin HY, Liu H, **Freed D**, Arora RC, Tian G. Pathological mechanism for delayed hyperenhancement of chronic scarred myocardium in contrast agent enhanced magnetic resonance imaging. *PLOS ONE*. 2014 May 6;9(5):e96463.
37. Ngo MA, Li Y, Neumann S, Durston M, Tian G, Dixon IMC, Arora RC, **Freed DH**. Human Mesenchymal Stem Cells Adopt a Myofibroblastic Phenotype *in vitro*: Comparison to Human Cardiac Myofibroblasts. *Mol Cell Biochem*. 2014 Jul;392(1-2):187-204.
38. Cheung A, White CW, Davis M, **Freed DH**. Temporary mechanical circulatory support for acute right ventricular failure: clinical outcomes of patients supported with the Impella RD and RP microaxial pumps. *J Heart Lung Transplant*. 2014 Aug;33(8):794-9.

39. Yeganeh B, Wiechec E, Ande SR, Sharma P, Moghadam AR, Post M, **Freed DH**, Hashemi M, Zeki AA, Ghavami S. Targeting the Mevalonate Cascade as a New Therapeutic Approach in Heart Disease, Cancer and Pulmonary Disease. *Pharmacology & Therapeutics*. 2014 Jul;143(1):87-110.
40. Kumar K, Singal R, Manji RA, Zarychanski R, Bell DD, **Freed DH**, Arora RC. The Benefits of 24/7 In-House Intensivist Coverage for the Prolonged Stay Cardiac Surgery Patient. *J Thorac Cardiovasc Surg*. 2014 Jul;148(1):290-7.
41. Ali AA, Downey P, Singh G, Qi W, George I, Takayama H, Kirtane A, Krishnan P, Zalewski A, **Freed D**, Large SR, Ashley EA, Leon MB, Bacchetta M, Ali ZA. Rat model of veno-arterial extracorporeal membrane oxygenation. *J Transl Med*. 2014 Feb 7;12:37.
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43. Rizkallah J, Shen S, Tischenko A, Zieroth S, **Freed DH**, Khadem A. Successful Ablation of Idiopathic Left Ventricular Tachycardia in an Adult Patient on ECMO. *Can J Cardiol*. 2013 Dec;29(12):1741.e17-19.
44. Nayak JG, White CW, Nates W, Sharda R, Horne D, Kaler K, Lytwyn M, Grocott HP, **Freed DH**, McGregor T. Laparoscopic Nephroureterectomy in a Patient with a Left Ventricular Assist Device. *Can Urol Assoc J*. 2013 Sep;7(9-10):E640-4.
45. Cheung P, Philipp R, **Freed DH**. Endovascular stenting for treatment of a left internal mammary artery pseudoaneurysm following redo-sternotomy: A case report. *Catheter Cardiovasc Interv*. 2013 Nov 1;82(5):778-81.
46. Elhami E, Dietz B, Xiang B, Deng J, Wang F, Chi C, Goertzen AL, Mzengeza S, **Freed D**, Arora RC, Tian G. Assessment of three techniques for delivering stem cells to the heart using PET-MR imaging. *EJNMMI Res*. 2013 Oct 28;3(1):72.
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50. Sharda R, Deutscher R, Christodoulou C, Horne D, **Freed DH**, McGregor T. Unanticipated Intra-operative finding of Pulmonary Artery Tumour Thromboembolism During Radical Nephrectomy and Caval Thrombectomy – Case Report and Management. *Can Urol Assoc J*. 2013 May-Jun;7(5-6):E381-5.
51. Farid S, Page A, Jenkins D, Jones MT, **Freed D**, Nashef SAM. FIASCO II: Failure to achieve a satisfactory cardiac outcome: The elimination of system errors. *Interact Cardiovasc Thorac Surg*. 2013 Jul;17(1):116-9.
52. Ali A, White CW, **Freed DH**, Ali Z, Large S. Ethicality of Heart Transplantation from Donation after Circulatory Death donors. *J Clin Exp Cardiol*. 2013, S9:006.
53. Muller A, **Freed D**, Dhalla N. Activation of proteases and changes in Na<sup>+</sup>-K<sup>+</sup> ATPase subunits in hearts subjected to ischemia-reperfusion. *J Appl Physiol*. 2013 Feb;114(3):351-60.

