

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MURRAY & POOLE ENTERPRISES, LTD.,

Petitioner,

v.

INSTITUT DE CARDIOLOGIE DE MONTREAL,

Patent Owner,

Case IPR2023-01064

Patent No. 11,400,063

DECLARATION OF HOSSEIN ARDEHALI, M.D., Ph.D.

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1. I, Dr. Hossein Ardehali, M.D., Ph.D., submit this expert declaration in the above-referenced proceeding in support of the Patent Owner's Preliminary Response.

2. This declaration demonstrates that the Petition for *inter partes* review does not show facts that support a person of ordinary skill in the art ("POSA") at the time of filing of the application for U.S. Patent No. 11,400,063 ("the '063 patent") would have found the claimed inventions obvious over the prior art and a POSA's knowledge. There was no expectation that a low dose of colchicine administered within 3 days of a percutaneous intervention without a loading dose would treat the patient and reduce the likelihood of future cardiovascular (CV) events, such as subsequent myocardial infarction.

I. PERSONAL BACKGROUND

3. I am currently the Director of the Center for Molecular Cardiology in the Feinberg Cardiovascular and Renal Research Institute at Northwestern University Medical Center. I am also currently the Thomas D. Spies Professor of Cardiac Metabolism as well as Professor of Medicine in Cardiology and Pharmacology. I served as the Director of the Medical Scientist Training Program at Northwestern University until April 2023.

4. I received my medical degree (MD) from Vanderbilt University in 1998, where I also received my Ph.D. in molecular physiology and biophysics in

1996. I completed my internal medicine residency and cardiology fellowship at Johns Hopkins Hospital in 2001 and 2004, respectively. I am board certified in Cardiovascular Disease from the American Board of Internal Medicine.

5. Throughout my career I have maintained an awareness of the developments in cardiovascular care and treatment, including as serving on editorial boards for journals including for example, PLoS ONE, Journal of the American Heart Association, Circulation Research, and the Journal of Clinical Investigation. I also served as an editor to a cardiovascular medicine textbook, the Manual of Cardiovascular Research Techniques. Additionally, I regularly serve as a journal reviewer for at least forty different journals. I am currently the Deputy Editor of the Journal of Clinical Investigation.

6. Importantly, I not only treat patients in the clinic and teach future cardiologists, but I have also maintained a robust research practice. Since 2004, I have been the Principal Investigator, Co-Principal Investigator, or Mentor to the Principal Investigator on more than 35 grant awarded studies.

7. I am a named author on 112 articles and 7 book chapters, and I have been an invited lecturer numerous times across the globe. Moreover, I have served in multiple leadership roles for committees and organizations devoted to advancing cardiovascular medicine, including multiple leadership roles at the American Heart Association and International Society for Heart Research. I have also been inducted

into the honor societies of the American Society for Clinical Investigation (ASCI) and Association of American Physicians (AAP). I served as the Secretary-Vice President for the ASCI in 2019, and then as the Vice President, President Elect and President of the Society in 2019-22.

8. I have won numerous prestigious awards and honors, including for example, the Jeremiah Stamler Distinguished Young Investigator Award (2005); the Schweppe Foundation Research Award (2006); the Central Society for Clinical Research Early Career Development Award (2009); and the Most Valuable Player Award, AHA BCVS Council (2010). I have also been awarded the Teaching Award given by Northwestern University medical students in 2009. I have also twice been nominated for the highly prestigious Presidential Early Career Award for Scientists and Engineers (PECAS) by the National Heart Lung, Blood Institute.

9. A complete recitation of my education, employment, research, and professional activities are listed in my curriculum vitae, which is attached as **Appendix A**.

II. MATERIALS CONSIDERED

10. The opinions set forth herein are based on my education, training, professional experience, documents I reviewed, the Declaration of Dr. Ridker, and information available to me at present. I have reviewed and considered the documents and materials cited in this declaration, the Petition, the declaration of Dr.

Ridker, and those listed in **Appendix B**. I reserve the right to modify, expand, or otherwise amend my opinions in view of new information, and in response to any additional reports or testimony.

III. LEGAL STANDARD

11. I am not an attorney, but I have been informed of certain patent law principles by counsel.

12. I understand from counsel that a patent is interpreted from the perspective of a POSA at the time the patent was filed. I understand that Dr. Ridker opines that a POSA would have an M.D. degree, be board certified in the treatment of cardiovascular disease, have 3-5 years' experience treating cardiovascular disease, and would have been "aware of research relating to cardiovascular disease progression, including the role of inflammatory pathways in secondary cardiovascular events."¹ I disagree with Dr. Ridker's definition as being too narrow. In my opinion, a POSA for the '063 patent would be an M.D. with training and 3-5 years of experience in treating cardiovascular disease. Regardless of the definition the Board adopts, my opinions here remain the same.

13. I understand from counsel that the terms in a patent's claim are typically given their plain and ordinary meaning as understood by a POSA when read in view

¹ EX1049 at ¶ 89.

of the specification and prosecution history. I further understand from counsel that a claim's preamble is limiting when it is necessary to give life to the invention or when the preamble is material to its patentability.

14. I understand from counsel that for a reference to "anticipate" a patent claim, the reference must firstly be prior art according to the patent laws, which I understand must be a publication available to the public before the patent's priority date, or if authored by the inventor, but have been published more than one year before the patent's priority date. I further understand from counsel that if the reference is prior art, then it must also disclose each of the limitations to anticipate a claim.

15. I have been informed by counsel that the assessment of whether a patent claim is "obvious" is a factual inquiry with factors including: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. Where a party asserts a combination of references, there must have been a motivation or reason for a POSA to combine the teachings from those references with a reasonable expectation of success of arriving at the claimed subject matter.

IV. STATE OF THE ART

16. Dr. Ridker outlines the typical course of events from a myocardial infarction (MI) that are necessary to treat a patient, which can include percutaneous coronary intervention (PCI).² I generally agree with Dr. Ridker's recounting of the course of treatment, and the need to improve standard therapies before the claimed inventions.³

A. Colchicine

17. Colchicine is a potent, orally-administered anti-inflammatory medication that has long been used.⁴ Colchicine has been indicated for the treatment of gout, familial Mediterranean Fever (FMF), and pericarditis.⁵ The anti-inflammatory actions of colchicine were understood by a POSA as of 2019.

18. The use of colchicine in treating cardiovascular disease is well-understood, including to treat acute pericarditis and myocardial infarction (MI). Physicians would have known that using colchicine in this context relied on a

² EX1049 at ¶¶ 22-24.

³ *Id.*

⁴ EX1001 at 1:28-30.

⁵ *Id.* at 1:43-44.

loading dose followed by maintenance doses.⁶ Thus, a POSA would have understood that colchicine may be effective in the treatment of CV events, including the acute context due to its anti-inflammatory action, but that a loading dose is necessary to initiate the desired response.

B. The Nidorf LoDoCo study

19. Because of the known anti-inflammatory properties of colchicine, and use in treating pericarditis, some POSAs hypothesized that it may have a variety of other uses. By 2013, there were several investigations relating to colchicine's use for cardiovascular indications including by Dr. Nidorf and colleagues who conducted the Low Dose Colchicine for Secondary Prevention of Cardiovascular Disease (LoDoCo) trial.⁷

20. The primary investigated outcome of the LoDoCo study was the composite incidence of acute coronary syndrome, out-of-hospital cardiac arrest, or

⁶ See, e.g., EX1040 at 1396 (using a loading dose of 2 mg to initiate treatment followed by 0.5 mg maintenance dose of five days after MI); EX2007 at 410 (patients receiving a loading dose of 1-2 mg on day one followed by maintenance dose of 0.5-1.0 mg thereafter); EX2005 at 2013 (administering a loading dose of colchicine followed by a maintenance dose); EX2006.

⁷ See EX2002; EX1020.

noncardioembolic ischemic stroke.⁸ In the study, patients with stable coronary disease receiving aspirin and/or clopidogrel and statins were randomly assigned to 0.5 mg colchicine per day or no colchicine.⁹

21. The LoDoCo study was a small study, it only enrolled 532 patients total with 282 randomized to colchicine treatment and only 243 of those patients that did not withdraw early.¹⁰ The study was not placebo-controlled.¹¹

22. The LoDoCo study investigated the use of low dose colchicine in patients with stable coronary disease, rather than patients with existing acute coronary syndromes (“ACS”).¹² LoDoCo did evaluate colchicine’s impact on the risk of experiencing ACS, but as Dr. Ridker himself acknowledges “the addition of colchicine 0.5 mg/day to standard therapy *in patients with stable coronary disease* significantly reduced the risk of a cardiovascular event.”¹³ Patients with history of

⁸ EX2002 at Outcomes; EX1020 at 405.

⁹ EX1020 at 405.

¹⁰ EX1001 at 1:58-59.

¹¹ *Id.*

¹² *Compare* EX1020 at 406-407 with EX1049 at ¶ 27.

¹³ EX1020 at 408 (emphasis added); EX1049 at ¶ 33 (admitting “LoDoCo started treatment after CAD (including MI) had been stable for at least 6 months”).

MI have a higher risk of recurrent CV events than patients who have stable coronary disease, and are thus a patient population that raises separate and additional concerns.

23. The LoDoCo trial also does not instruct whether or not to use a loading dose of colchicine. A POSA would have expected a loading dose of colchicine would be useful in initiating the anti-inflammatory action.¹⁴ Indeed, Nidorf 2013 explains that “short-term use of low-dose colchicine has been found to have no effect on stent-related disease.”¹⁵

24. While the primary outcome of the LoDoCo trial was the composite incidence of acute coronary syndrome, out-of-hospital cardiac arrest, or noncardioembolic ischemic stroke, the purported “reduction in the primary outcome was largely driven by the reduction in the number of patients presenting with ACS....”¹⁶ LoDoCo admittedly “has a number of limitations,” including the study design that “may be subject to outcome ascertainment and reporting bias.”¹⁷

¹⁴ See, e.g., EX1040 at 1396; EX2007 at 410; EX2005 at 2013; EX2006.

¹⁵ EX1040 at 404-405 (citing EX2009).

¹⁶ *Id.* at 408.

¹⁷ *Id.* at 410.

C. COLCOT Clinical Study

25. The Colchicine Cardiovascular Outcomes Trial (COLCOT) also tested long-term use of a low dose of colchicine to reduce the risk of recurrent CV events, but was specific to MI patients within 30 days prior to treatment.¹⁸ Like LoDoCo, the COLCOT trial did not investigate the effect of low dose colchicine on patients unless they are stabilized, thus specifically excluding patients in the acute ACS setting.¹⁹ Additionally, the COLCOT study also does not teach a POSA to exclude a loading dose of colchicine, which would have been expected to be useful to initiate the anti-inflammatory action of the drug.²⁰

26. The COLCOT study enrolled 4745 patients across 167 facilities.²¹ The data was reported to Dr. Tardif, the inventor of the '063 patent, and analyzed in 2019 and 2020.²² Following that analysis, Dr. Tardif, along with his colleagues, published an article in the New England Journal of Medicine (“Tardif 2019”).²³ In the analysis,

¹⁸ EX1006 at 4-5.

¹⁹ Ex1001 at 2:4-7.

²⁰ *See, e.g.*, EX1040 at 1396; EX2007 at 410; EX2005 at 2013; EX2006.

²¹ EX1022 at 2497-2498.

²² EX2011 at ¶ 20.

²³ *See* EX1022.

Dr. Tardif surprisingly discovered that the COLCOT data also showed an opportunity for patients who had experienced an MI to have an improved course of treatment following PCI, and he published those findings in the follow-up Bouabdallaoui reference, as well as the patent application that issued as the '063 patent.²⁴

D. '063 Patent and prosecution history

27. As briefly described above, Dr. Tardif's surprising discovery from the COLCOT trial data ultimately resulted in the '063 patent. As well as authoring the Tardif 2019 article, Dr. Tardif also caused the U.S. Provisional Patent Application No. 62/935,865 to be filed in November 2019, which included certain information relating to the COLCOT study.²⁵ On October 20, 2020, Dr. Tardif caused U.S. Provisional Patent Application No. 63/093,988 to be filed, followed by U.S. Patent Application No. 17/097,285 ("the '285 application") on November 13, 2020.²⁶ The '285 application included additional information from the COLCOT data that was consistent with the two previous provisional applications.²⁷

²⁴ See EX. 1005; EX. 1002.

²⁵ EX2011 at ¶ 22.

²⁶ *Id.*; EX1002.

²⁷ EX2011 at ¶ 22-25.

28. During prosecution, the Examiner was provided Hennessey 2019 (reporting on LoDoCo and substantively the same as Nidorf 2013), Tardif 2019, Bouabdallaoui, and the COLCOT trial protocols.²⁸ On August 2, 2022, the Examiner issued the '063 patent from the '285 application. Notably, the Examiner concluded “[o]ne of ordinary skill would not have found it obvious to treat [MI] patients... who have also been treated with primary [PCI]... without a loading dose of colchicine. There is no motivation to delete the loading dose.”²⁹

V. NO SUPPORT THAT POSA WOULD HAVE FOUND CLAIMED INVENTION ANTICIPATED

29. I understand from counsel that Petitioner alleges that the claims of the '063 patent are anticipated by Bouabdallaoui, and that claims 27, 29-36, and 39 are anticipated by the COLCOT Protocol. I disagree with both positions.

30. I understand from counsel that Bouabdallaoui is not prior art, because it is a publication authored by the inventor less than one year before the priority date by the inventor or by another who obtained the subject matter disclosed directly from the inventor. Counsel have asked me to evaluate whether a POSA would regard Dr. Tardif as the author of the Bouabdallaoui reference. It is my opinion that a POSA would regard Dr. Tardif as the author.

²⁸ EX1002 at 75-77.

²⁹ EX1002 at 398.

31. In medical publications, there are a variety of ways and conventions that the authors may be listed. In most medical publications, the first named author is not indicative of the lead author or investigator for the particular research reported. Rather, a lead author/investigator may choose to list the author alphabetically, or give a mentee the opportunity to be the first-named in recognition of their work. If, however, a POSA wanted to discover who was responsible for the article, its research, and protocols, she would look to the corresponding author. In the Bouabdallaoui article, the corresponding author is Dr. Tardif, who is also the sole inventor of the '063 patent. Therefore, it is my opinion that a POSA would regard Dr. Tardif as the author of Bouabdallaoui and the other named authors as contributors to the research. Therefore, the Bouabdallaoui article is either an article by the inventor, Dr. Tardif, or the subject matter of the article was obtained directly from him, and thus my understanding is the article is not prior art that anticipates the '063 patent.

32. The COLCOT Protocol also does not anticipate claims 27, 29-36, and 39. While Petitioner uses a different version of the COLCOT Protocol here, I understand the Examiner was provided a substantially similar version, one that was more up-to-date if anything.³⁰ Importantly, a POSA would understand claims 27, 29-

³⁰ EX1002 at 7-53.

36, and 39 to be directed to methods of treatment. However, the COLCOT Protocol provided no information regarding the effect of treatment according to the dosing regimen described therein.³¹ That is plainly logical because the COLCOT Protocol was the method by which Dr. Tardif and colleagues would evaluate whether there even was a benefit to early intervention with colchicine. Thus, a POSA would not understand that the limitations of these claims could have even been met until the results from COLCOT were received and analyzed.

VI. NO SUPPORT THAT A POSA WOULD HAVE FOUND THE CLAIMED INVENTION OBVIOUS

33. It is my understanding from counsel that Petitioner asserts that claims 1-50 would have been obvious based on Nidorf in view of COLCOT Protocol, ESC Guidelines, and COLCRYs (Ground 3) and that claims 1-26, 28, and 40-50 would have been obvious based on Bouabdallaoui in view of COLCRYs (Ground 4). As an initial matter, because Ground 4 asserted by Petitioner requires Bouabdallaoui, which I understand is not prior art as discussed above, I understand that Bouabdallaoui cannot make obvious any claims of the '063 patent. Further, it is my opinion that a POSA would not have found the claimed invention described by the '063 patent obvious in view of either combination asserted by Petitioner.

³¹ See EX1006.

34. I understand from counsel that Petitioner disputes the proper construction of certain claim terms. I have adopted the constructions provided to me by counsel, specifically regarding “reducing the risk of stroke in a patient after having an MI” of claim 27 and “wherein the patient is at a lower risk of a cardiovascular event” of claims 8-11 and 20-23. I have been informed by counsel that the claim limitations in the preambles of claims 8-11, 20-23, and 27 are limiting, and I have been asked to assume they are. It is my opinion, that when read by a POSA, claim 27 and its dependent claims are directed to achieving the result of “reducing the risk of stroke in a patient after having an MI.” Similarly, when read by a POSA, claims 8-11 and 20-23 are directed to the recited result of “wherein the patient is at a lower risk of a cardiovascular event.” Moreover, I understand from the prosecution history that the “reducing the risk of stroke in a patient after having an MI” was critical to overcome the prior art.³²

³² EX1002 at 399 (“With respect to claims 29-31, the closest prior art also appears to be [Hennessy], outlined above. The reference does not teach, show, suggest or make obvious the instant method of reducing the risk of a stroke in a patient having had a [MI] by the administration of daily low dose colchicine within about 30 days of the [MI].”).

35. It is my opinion that Petitioner, and their expert, Dr. Ridker, failed to consider certain critical claim limitations in its analysis of Ground 3. I discuss each failure and the nonobviousness of claims 1-50 in turn below.

A. There was no reasonable expectation of success in using low-dose colchicine without a loading dose, and no motivation to remove the loading dose

36. Dr. Ridker opines that claims 1-50 would have been obvious from Nidorf, COLCOT Protocol, and ESC Guidelines. I disagree. Critically, Dr. Ridker's analysis neglects whole claim limitations, including those that were part of Dr. Tardif's surprising discovery. For example, Dr. Ridker neglects to assess whether the prior art even taught administering low-dose colchicine without a loading dose.³³

37. A POSA would not have had a reasonable expectation of success in treating patients without a loading dose, because the Nidorf and COLCOT Protocols both required the patient to first be stabilized. Therefore, a POSA would understand that a stabilized patient would already have a reduction in inflammation, and the low dose would be acting on maintaining that reduction and likelihood of recurrence. There would not have been a reasonable expectation that the low dose without a loading dose would reduce inflammation in the acute setting that Dr. Tardif surprisingly discovered here.

³³ EX1049 at ¶¶ 142-144.

38. Although some studies investigated “lower doses” of colchicine as a strategy for mitigating certain side effects, these studies still taught a POSA to use a loading dose.³⁴ Indeed, the use of a loading dose regimen remains in use in more recent studies.³⁵ Thus, a POSA would expect that a loading dose was necessary for colchicine treatments within at least the first five days following an acute disorder, and more specifically necessary for treatment of acute cardiovascular events.³⁶

39. Similarly, Nidorf reports on the LoDoCo study, which did not administer low doses of colchicine to patients until stable for six months after CV event.³⁷ A POSA would therefore understand that the long-time of stability would not have reasonably expected that one could remove a loading dose from a patient shortly after their MI, because the inflammation would be expected to be much more

³⁴ See, e.g. EX2010 (teaching a “low-dose arm of 1.2 mg followed by 0.6 mg in 1 hr and a “high-dose” arm of 1.2 mg followed by 0.6 mg every hour for six hr).

³⁵ EX2008 (using 0.5 mg thrice daily for five days followed by 0.5 mg twice daily to treat COVID-19).

³⁶ See, e.g., EX1040 at 1396; EX2007 at 410; EX2005 at 2013; EX2006.

³⁷ EX1020 at 405.

severe. Indeed, Nidorf reported that previous studies of “short-term use of low-dose colchicine has been found to have no effect on stent-related diseases.”³⁸

40. Petitioner incorrectly asserts that Nidorf and the COLCOT Protocol teach administering a low dose of colchicine without a loading dose.³⁹ However, rather than teaching that deviation from the previous standard, those studies were silent regarding use of a loading dose.⁴⁰ Thus, a POSA would not assume one way or the other regarding the use of a loading dose from these references, and this claim limitation is not taught in the prior art. In any event, as discussed above, the patients in both Nidorf and the COLCOT Protocol involved patients that were stable, and a POSA would not have made any determinations about excluding a loading dose based on patients that are stable.

41. Simply, Petitioner and their expert have not shown that this limitation was present in the prior art, and they cannot. Their oversight resulted in omitting any analysis of a POSA’s reasonable expectation of success or motivation regarding the “without pre-loading” limitations. Regardless, because the references do not teach any removal of a loading dose, any motivation to remove the loading dose so near

³⁸ *Id.* at 404-405 (citing EX2009).

³⁹ Petition at 37.

⁴⁰ *See* EX1006; EX1020.

an MI, or show any reasonable expectation of success in doing so, this claim limitation is nonobvious.

42. Moreover, the Examiner had the COLCOT Protocol and Hennessy (which reports on LoDoCo and is substantively the same information as Nidorf 2013) during prosecution. However, even with that reference, the Examiner still concluded that, among other limitations, the “without pre-loading” limitation overcame the prior art.⁴¹

B. There is no motivation to administer low-dose colchicine to patients with a PCI

43. Similar to the omissions regarding “without pre-loading,” Petitioner and its expert also neglect to consider the PCI limitation, which applies to claims 1-7, 9, 12-19, 21, and 24-26. Tellingly, Dr. Ridker refers to this limitation only in passing by providing it as an example of post-MI emergency management options disclosed in the COLCOT Protocol.⁴² While PCI is a common treatment post-MI, it is one of multiple approaches, thus, a POSA would not conclude from the prior art that there was a motivation to administer low-dose colchicine to post-MI patients that have undergone a PCI.

⁴¹ EX1002 at 398.

⁴² EX1049 at ¶ 146.

44. Indeed, the examiner specifically concluded that a POSA would not have found it obvious to treat post-MI patients with a PCI with low-dose colchicine without a loading dose.⁴³ I agree with that conclusion. A POSA would not have had any motivation to treat this specific class of patients with low-dose colchicine without a loading dose because there was no teaching or suggestion in the prior art that doing so would result in a reduction of CV recurrence.⁴⁴

C. There was no reasonable expectation that low-dose colchicine administered within 3 days following MI would reduce risk of CV events.

45. Dr. Ridker alleges that the only limitation from claim 1, 8, and 27 not disclosed in Nidorf is starting treatment “within about 3 days” or “within 30 days” of MI.⁴⁵ I agree with Dr. Ridker regarding the teachings of Nidorf in this regard. However, I disagree with Dr. Ridker that this limitation would have been obvious in view of Nidorf and the COLCOT Protocol. Dr. Ridker’s analysis is flawed, and until Dr. Tardif’s surprising discovery, a POSA would not have expected to reduce CV events with low-dose colchicine without a pre-loading dose initiated within 3 days following an MI and PCI treatment.

⁴³ EX1002 at 398.

⁴⁴ *See, e.g.*, EX1040.

⁴⁵ EX1049 at ¶ 145.

46. Importantly, I understand from counsel that the unique combination of limitations must be considered, rather than each limitation on its own. Tellingly, Dr. Ridker devotes a mere 3.5 pages to all independent claim limitations other than 3 days post-MI and 15.5 pages specifically to the 3 days post-MI limitation.⁴⁶ Indeed, the Examiner found that unique combination of the low-dose colchicine administered within 3 days post-MI and after PCI treatment to be nonobvious.⁴⁷ I agree with the Examiner's conclusion, that this unique combination is the surprising invention to which Dr. Tardif was granted a patent.

47. Even if taken in isolation, initiating colchicine treatment according to the claimed method within 3 days post-MI is nonobvious. The Nidorf reference, which reports the findings of LoDoCo, only administered the low dose of colchicine to patients that had been stable for six months.⁴⁸ Thus, a POSA would not have expected the same or similar effectiveness at within 3 days. The CANTOS study, which Dr. Ridker does not list in his combination of references, taught that anti-inflammatory treatment initiated after 30 days post-MI reduced the recurrence of a

⁴⁶ *Id.* at Sec. VIII.A.1.b. – 2.

⁴⁷ EX1002 at 394-400.

⁴⁸ EX1020 at 405.

CV event.⁴⁹ However, that study was not specific to colchicine, and again, had patients stabilized for 30 days post-MI.⁵⁰ The ESC Guidelines would also not have led a POSA to expect success with the '063 patent's limitation of administering colchicine within 3 days. The ESC Guidelines at the time recommended initiating secondary preventative therapy at hospital discharge.⁵¹ However, Dr. Ridker neglects to recognize that the recommendation was based off the treatments existing at the time, which were entirely unrelated to colchicine treatment.⁵²

48. Moreover, Dr. Ridker neglects to include the fact that statin initiation recommended in the ESC Guidelines are for high intensity statins.⁵³ A POSA would have known that these high intensity statins come in the form of atorvastatin or rosuvastatin, which have strengths of 40-80 mg and 20-40 mg, respectively. Based on that knowledge, a POSA would not have reasonably expected that an anti-inflammatory dose of 0.5 mg would lead to similar improvements in reducing future CV events. Thus, a POSA would not have reasonably expected that simply because

⁴⁹ See EX2003.

⁵⁰ *Id.*

⁵¹ EX1009 at 151.

⁵² EX1049 at ¶¶ 147-148.

⁵³ EX1009 at 151.

one could successfully initiate one treatment within three days that a completely different treatment—low-dose colchicine—could also be initiated on that schedule.

49. Dr. Ridker's reliance on the COLCOT Protocol is also misplaced. The COLCOT Protocol disclosed initiating low-dose colchicine within 30 days of an MI.⁵⁴ However, as I described above, the COLCOT Protocol was merely a protocol, and did not disclose any results.⁵⁵ That study was typical for determining the effective dosing regimen when it is unknown. The researcher will often set one variable group at a target expected to work (e.g. 30 days post-MI) and work down to find the lower limit. Based on the prior art, including the COLCOT Protocol, a POSA would not have had a reasonable expectation that low-dose colchicine treatment initiated at 30 days post-MI would also be effective within 3 days post-MI, which is what is recited by claims 1-26 and 40-50.

D. There was no motivation to combine references that colchicine treatment would reduce risk of stroke as recited in claim 27, nor a reasonable expectation of success

50. Petitioner, and their expert, also alleges that claims 27-39 are obvious over Nidorf in view of COLCOT and ESC Guidelines. However, neither Dr. Ridker

⁵⁴ EX1006.

⁵⁵ *See supra.* ¶ 32.

nor Petitioner explained what motivation a POSA would have had to combine these references. It is my opinion that no such motivation existed.

51. Even if each claim limitation is present in disparate prior art references, I understand from counsel that the Petitioner must still show what motivation a POSA would have had to combine those references and arrive at the claimed invention. Without a motivation to combine teachings, a POSA would not have considered combining the references except with the benefit of Dr. Tardif's discovery.

52. A POSA would not have had a reasonable expectation of success in reducing stroke by administering low-dose colchicine within 30 days post-MI. COLCRYS never taught administering colchicine for reducing stroke, and does so for different purposes than those claimed by the '063 patent.⁵⁶ Thus, a POSA would not have a reasonable expectation regarding the effectiveness of administering colchicine to reduce stroke in patients 30 days post-MI.

53. A POSA also would not have a reasonable expectation of success from the ESC Guidelines because those teachings are far too general and did not disclose anything specific to colchicine and its benefits for reducing stroke. The ESC Guidelines actually taught that several drug interventions similar to the colchicine

⁵⁶ See EX1016.

regimen are contraindicated for certain patients who have had an MI. For example, the ESC Guidelines explain that antiarrhythmics are contraindicated for MI patients with atrial fibrillation (AF) risk or patients at risk for ventricular arrhythmias and conduction disturbances in the acute MI phase.⁵⁷ A POSA would have known that anti-inflammatory drugs, like colchicine, have similar effects and may not reduce stroke for these patients. Thus, a POSA would not expect success in reducing stroke with the claimed colchicine regimen.

54. As I explained above, Nidorf reports on the LoDoCo study, which a POSA would recognize has limited utility due to its relatively small sample size and lack of a placebo control.⁵⁸ Even if a POSA did take some expectations from Nidorf, there is no teaching regarding colchicine 30 days post-MI reducing the risk of stroke.

55. Similarly, the COLCOT Protocol does not show that administration of low-dose colchicine within 30 days post-MI reduces the risk of stroke. The COLCOT Protocol merely included stroke as an endpoint that was evaluated by the study but did not include any results.⁵⁹ Thus, a POSA would not have drawn a

⁵⁷ See EX1009 at 48-50.

⁵⁸ *Supra.* at ¶ 21.

⁵⁹ Compare EX1006 with EX. 2004.

reasonable expectation of the success of that particular endpoint merely from the Protocol.

56. The discovery that administering colchicine in a low dose, without pre-loading, in a patient within 30 days post-MI would result in a reduction of stroke was never taught and had no reasonable expectation of success. A POSA would have expected a loading dose was necessary to reduce the risk of a stroke in a patient, because the POSA would not have expected a sufficient anti-inflammatory response without such a loading dose.⁶⁰

E. Secondary Considerations

57. Claims 1-50 of the '063 patent provide an unexpected benefit in the treatment of MI patients that have undergone a PCI and are treated with low dose colchicine. Dr. Tardif's discovery that patients undergoing a PCI that were administered daily low-dose colchicine, with no loading dose, either within 3 days post-MI or within 30 days post-MI saw a 25% reduction in the risk of future CV event, including stroke.⁶¹

⁶⁰ EX1040; EX2009 (teaching that treatment with 0.6 mg twice daily colchicine within 24 hr post-angioplasty treatment was "ineffective for preventing restenosis after coronary angioplasty").

⁶¹ EX1001 at 25:55-26:9.

58. More specifically, the ability to administer low-dose colchicine according to claims 1-26 and 40-50 (within 3 days post-MI in PCI patients) provided the unexpected benefit of reducing the risk of future CV events. This unexpected result, in part, led to the '063 patent. Thus, even if Petitioner has shown a POSA could be motivated to combine the teaching of the prior art to arrive at the claimed invention, the unexpected benefit is sufficient to overcome any showing of obviousness.

59. Moreover, Dr. Tardif's invention led to a benefit to patients not previously identified. As the Examiner noted, the prior art did not show or support the benefit of reducing stroke in patients administered low-dose colchicine according to claims 27-39.⁶² Indeed, Dr. Tardif's metanalysis of the data from four randomized controlled trials, surprisingly showed there was a 62% attenuated risk reduction in stroke for patients administered low-dose colchicine according to claims 27-39.⁶³ This clear benefit does not show that a POSA would have found the invention obvious, rather, because the benefit is so obvious but was never done, a POSA would have found the invention disclosed in claims 27-39 surprising.

⁶² EX1002 at 398-399.

⁶³ EX1001 at 26:1-5.

VII. CONCLUSION

60. For the foregoing reasons, it is my opinion that the claims of the '063 patent are not anticipated and a POSA would not have found them obvious in view of the prior art.

61. This declaration is based on information known to me as of the date I signed this declaration, and I reserve the right to amend or supplement this declaration in view of any additional discovery, documents, information, declarations, and/or testimony that I receive after issuance of this declaration. I also reserve the right to rebut opinions and testimony offered by witnesses for Petitioner.



Hossein Ardehali, MD, PhD

SHDOCS:220324120.1

Appendix A

Hossein Ardehali, MD, PhD

Date of Birth: December 21, 1968

Citizenship: United States

Home Address: 1259 W Wrightwood Ave
Chicago, IL 60614

Phone: 630-215-9461

Business Address: Northwestern University Medical Center
SQBRC 8-521
303 E Superior Street
Chicago, IL 60611

Business Phone: 312-503-2342
312-503-2296

Business Fax: 312-503-0137

Email: h-ardehali@northwestern.edu

EDUCATION

Date awarded	Institution	Degree
Discipline		
6/1990	University of Utah, Salt Lake City, Utah	B.S.
Computer Science		
5/1996	Vanderbilt University School of Medicine	Ph.D.
Molecular Physiology		
		and Biophysics
5/1998	Vanderbilt University School of Medicine	M.D.
(MSTP program)		

TRAINING

Dates	Institution	Specialty
7/2001-6/2004		The Johns Hopkins Hospital
	Cardiology Fellow	
7/1999-6/2001	The Johns Hopkins Hospital	Internal Medicine
Resident Physician		
7/1998-7/1999	The Johns Hopkins Hospital	Internal Medicine
Intern		
3/1996-11/1996	Vanderbilt University	
	Postdoctoral Fellow	

LICENSURE/CERTIFICATION

Board certification:

Diplomate	American Board of Internal Medicine	2001
	Internal Medicine	
Diplomate	American Board of Internal Medicine	2005, 2015
	Cardiovascular Disease	

Licensure:

Maryland Medical License	2001-2006
Illinois Medical License	2005-present
DEA Controlled Substance Registration	2001-present

ACADEMIC APPOINTMENTS

Dates	Title	Institution
	Department	
11/19-present	Thomas D. Spies Professor	School of Medicine
	of Cardiac Metabolism	Northwestern University
09/17-present	Director, Medical Scientist	School of Medicine
	Training Program	Northwestern University
06/16-present	Director, Center for	School of Medicine

	Mol. Cardiology	Northwestern University
09/2014-present	Professor with	School of Medicine
Medicine	tenure	Northwestern University
09/2014-present	Professor with	School of Medicine
Pharmacology	tenure	Northwestern University
05/2013-2016	Visiting Professor	University of Wroclaw,
Cardiology		Wroclaw, Poland
09/12-9/17	Associate Director	Northwestern University
	and chair of	
	Admissions, MSTP	
09/10-09/14	Associate Professor	School of Medicine
Medicine	with tenure	Northwestern University
09/10-09/14	Associate Professor	School of Medicine
Mol. Pharm &	with tenure	Northwestern university Biol
Chemistry		
12/2004-8/10	Assistant Professor	School of Medicine
Medicine		Northwestern University
07/2005-8/10	Assistant Professor	School of Medicine
Mol. Pharm &		Northwestern university Biol
Chemistry		

7/2004-12/2004 Instructor
Medicine

School of Medicine

Johns Hopkins University

HOSPITAL APPOINTMENTS

Dates	Institution
01/2005-Present	Northwestern Memorial Hospital
7/2004-12/2004	Johns Hopkins University School of Medicine

HONORS and AWARDS

Dates	Name of Award
1986-1990	Dean's Honor Role, every quarter
1987-1990	Alpha Epsilon Delta Premedical Honor Society
1988-1990	Computer Science Departmental Award, University of Utah
1990	Cum Laude, University of Utah
1991-1998	Vanderbilt MSTP Scholarship
1991-1998	Microbial Defense (MD) Honor Society
	Vanderbilt's honor society for excellence in microbiology
7/1996	Vanderbilt MSTP award to the National MSTP Conference, Aspen, CO
1998-2001	Sigma Xi Honor Society

3/2001 Pfizer Travel award to the American College of Cardiology, Atlanta, GA

5/2003 Finalist for annual Basic Science Research Award
Dept. of Medicine, Johns Hopkins University

2003 Travel Award to the American Heart Association, Orlando, FL

2003 Young Investigator Award
American Heart Association Council on Basic Cardiovascular Sciences

2003 National AstraZeneca Young Investigator Award, First place

2004 GSK International Competitive Grant Awards for Young Investigators

2004 Johns Hopkins Clinician Scientist Award

2005 Fellow, Northwestern University Searle Center for Teaching Excellence

2005 Northwestern Medical Foundation Young Investigator Award

2005 Jeremiah Stamler Distinguished Young Investigator Award

2006 Finalist, International Society for Heart Research Young Investigator Award

2006 Department of Medicine's Investigators Developing Excellence in Academics Award, (DOM-IDEA), Northwestern University

2006 The Schweppe Foundation Research Award

2006 Travel Award to the American Society of Clinical Investigation

2007 K Award Grant for the 2007 combined CSCR and MWAfMR meeting

2008 Nominated by the National Heart, Lung, Blood Institute for the Presidential Early Career Award for Scientists and Engineers (PECASE) Award

2008	Fellow, American Heart Association
2009	Central Society for Clinical Research Early Career Development Award
2009	Nominated by the National Heart, Lung, Blood Institute for the Presidential Early Career Award for Scientists and Engineers (PECASE) Award
2009	Teaching Award by Northwestern Medical Students
2010 Council	Most Valuable Player Award, American Heart Association BCVS
2011	AHA BCVS Annual Award for service and recruitment of FAHA
2011	Inducted into the American Society for Clinical Investigation
2016	Council member, American Society for Clinical Investigation
2017	Secretary-Treasurer, American Society for Clinical Investigation
2018	Inducted into Association of American Physicians
2019 President	Elected American Society for Clinical Investigation (ASCI) Vice-
2021	President, American Society for Clinical Investigation (ASCI)
2022	Deputy Editor, <i>Journal of Clinical Investigation</i>
2023 Ireland	Honorary Fellow, Association of Physicians of Great Britain and

PROFESSIONAL ORGANIZATION

Fellowship:

- 2005-present Fellow, American College of Cardiology
- 2007-present Fellow, American Heart Association

2019-present Fellow, International Society for Heart Research

Membership:

American Medical Student Association, 1990-98

American Medical Association, 1990-present

American Diabetes Association, 1996-98

American College of Cardiology, 2001-present

American Heart Association, 2002-present

Biophysical Society, 2003-2005

Central Society for Clinical Research, 2006-present

American Society for Clinical Investigation, 2012-present

International Society for Heart Research, 2013-present

Association of American Physicians, 2018-present

PROFESSIONAL ACTIVITIES:

INSTITUTIONAL SERVICE (Committees, Councils, Task Forces)

(b) Dates	Title	Institution
2002-03 University	Director of Clinical Fellows	Johns Hopkins
	Distinguished Speakers Series, Cardiology	
2002-03 University	Director of Cardiology Fellowship	Johns Hopkins

Conferences

2005-present Member, Cardiology Fellowship Selection Northwestern
University

Committee

2005 Member, Feinberg Cardiovascular Institute Northwestern
University

Director Search Committee

2005-2008 Member, MSTP admission Committee
Northwestern University

2005-present Co-organizer, Cardiology Grand Rounds Northwestern
University

2006-2015 Co-Director, Cardiology Fellowship
Northwestern University

Research

2006-present Member, Dept of Medicine Research Northwestern University
Council

2006-present Member, Dept of Medicine Fellows Northwestern
University

Research Task Force

2006-2009 Co-organizer, Dept of Medicine Junior
Northwestern University

Faculty Conferences

2006-2010 Associate Director, Physician Scientist Northwestern
University

Training Program

2008-present Member, Assistant Professors Research Northwestern
University

Committee

2009-2011 Member, Promotion & Tenure Task Force Northwestern
University

2010-present Member, Limited Submissions Advisory Northwestern
University

Committee

2010-present Member, Library Committee Meeting Northwestern University

2008-17 Chair, MSTP Admissions Committee Northwestern University

2010-14 Director, CV Genetics Program Northwestern University
and NMH Hospital

2012-present Member, Laboratory program Advisory Northwestern
University

Committee

2011-17 Associate Director, Medical Scientist Northwestern University
Training Program

2017-2023 Director, Medical Scientist Training
Northwestern University

Program
2015-present Director, Center for Molecular
Cardiology Northwestern University

TEACHING

Lectures and Classroom Teaching:

2016-present Co-Director, “Introduction to Pharmacology” course

2/2007-present Northwestern University “Molecular mechanism of drug
action” course

12/2004	Johns Hopkins Medical School Clinical Core Course
2003	Johns Hopkins Medical School second year Clinical rotation
1990	University of Utah Computer Graphics Course

Clinical Teaching:

2005-present Coronary Care Unit or Inpatient Rounds (2-3 months per year)

TRAINEES

Post doctoral Fellows:

<u>Name</u> <u>Position</u>	<u>Years in lab</u>	<u>Position in lab</u>	<u>Current</u>
Lin Sun, MD, PhD Professor, China	2006-2007	Postdoctoral fellow	
Rongxue Wu, MD, PhD	2007-present	Res. Assistant Professor	Assistant Prof, U of Chicago
Mike Burke, MD	2006-2008	Cardiology fellow	Assistant Prof, Emory University
Richard Fernandez, MD	2007-2008	Pediatric card fellow	
Kannan Mutharasan, MD Assistant Prof, NW	2007-present	Cardiology fellow	
Yoshihiko Ichikawa, MD Assistant Prof, Univ. of Tokyo	2007-2010	Postdoctoral fellow	
Anita Thakur, PhD Israel	2010-2013	Postdoctoral fellow	Fellow,
Tatsuya Sato, MD, PhD	2013-2016	Postdoctoral fellow	Asst

Professor,

Sapporo

Univ. of

Xiaoyan Yang, MD, PhD 2013-2016
Professor,

Postdoctoral fellow

Asst

UIC

E. Abdelwahid, MD, PhD 2013-2015
Instructor, NW

Res. Assistant Professor

Sumeyye Yar, PhD 2014-2016
Postdoc fellow,

Postdoctoral fellow

Netherlands

Hidemichi Kouzu, MD, PhD 2015-2018
Asst Professor,

Postdoctoral fellow

Univ. of

Sapporo

Paulina Stanczyk, PhD 2018-2020
fellow,

Postdoctoral fellow

Postdoc

Cardiff Univ.

Sam Man Lee, PhD 2018-2020
fellow,

Postdoctoral fellow

Postdoc

Australia

Shunsuki Miura, MD, PhD 2018-2022
Assistant Professor

Postdoctoral fellow

Akita Univ.,

Japan

Farnaz Keyhani-Nejad, PhD 2018-2022

Postdoctoral fellow

Navid Koleini, MD, PhD 2020-2021
fellow.

Postdoctoral fellow

Postdoc

Johns Hopkins

Yuki Tatekoshi, MD, PhD	2018-present	Postdoctoral fellow
Amir Mahmoodzadeh, PhD	2021-present	Postdoctoral fellow
Mohammad Keykhaei, MD	2021-present	Postdoctoral fellow
Maryam Balibegloo, MD	2022-present	Postdoctoral fellow
Zeinab Najafi, Pharm.D.	2022-present	Postdoctoral fellow
Melika Shafeghat, MD	2022-present	Postdoctoral fellow

Graduate students:

<u>Name</u>	<u>Years in lab</u>	<u>Position in lab</u>
Eugene Wyatt	2006-2012	Graduate student
Amy Rines	2007-2013	Graduate student

MSTP students:

<u>Name</u>	<u>Years in lab</u>	<u>Position in lab</u>
Marina Bayeva	2008-2012	MSTP student
Jimmy Chang	2011-present	MSTP student
Konrad Sawicki	2013-2015	MSTP student
Jason Shapiro	2014-2017	MSTP student
Adam DeJesus	2015-present	MSTP student

Rotating graduate students:

<u>Name</u>	<u>Years in lab</u>	<u>Position in lab</u>
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Shetha Shukair	2005	Rotating graduate student
Kenji Wellman	2006	Rotating graduate student
Lewis Dore	2008	Rotating graduate student
Sinyi Kong	2010	Rotating graduate student
Elizabeth Tarasewicz	2010	Rotating graduate student
Daniel Levin	2011	Rotating graduate student
Funien Tsai	2012	Rotating graduate student
Anthony Leonardi	2013	Rotating graduate student
Simona Morochnik	2015	Rotating graduate student
Young Ruck Chung	2017	Rotating graduate student

Rotating MSTP students:

<u>Name</u>	<u>Years in lab</u>	<u>Position in lab</u>
Chris Brooks	2006	Rotating MSTP student
Marisa Jackson	2007	Rotating MSTP student
Betty Kong	2007	Rotating MSTP student
Oyinlolu Adeyanju	2008	Rotating MSTP student
David Escobar	2008	Rotating MSTP student
Adam De Jesus	2014	Rotating MSTP student

Medical students:

<u>Name</u>	<u>Years in lab</u>	<u>Position in lab</u>
Elliott Lieberman	2006	UIC medical student

Farzad Moazed student	2005	Northwestern Univ. medical
George Ochenjele student	2007	Northwestern Univ. medical
James Flaherty student	2008	Northwestern Univ. medical
Grant Senyei medical student	2012	Northwestern Univ.

Thesis committees:

Shetha Shukair

Betty Kong (MSTP)

David Escobar (MSTP)

[Simran Singh Sabharwal](#)

[Jacqueline Schriewer](#)

Anton Ludvik

Dipal Patel (MSTP)

Shuang Zhang

Andrew Chiu (MSTP)

Nina Calantone (MSTP)

Prathana Dalal (MSTP)

Sherry Lee (MSTP)

Jose-Marc Technor (MSTP)

Dalton Kim (MSTP)

EXTRAMURAL MEMBERSHIP

Organization of Meetings:

2005-present Chicago Mitochondrial Club (composed of mitochondrial scientists from around the city of Chicago)

6/2004-2006 National American Heart Association Annual Conference
Planning Committee

Conference chairs/Moderator:

2005	American Heart Association Scientific Sessions Featured Research: Mitochondrial Function & Cardioprotection
2005	American Heart Association Scientific Sessions Featured Research: Biology of Myocardial Ischemia and Cardioprotection II
2006	American Heart Association Scientific Sessions Biology of Myocardial Ischemia and Cardioprotection II
2010	American Heart Association Scientific Sessions Thomas Smith Memorial Lecture: Novel Regulators of Hypertrophy
2011	American Heart Association Scientific Sessions
2012	American Heart Association Basic Cardiovascular Sciences Annual Meeting
2012	American Heart Association Scientific Sessions
2013	American Heart Association Basic Cardiovascular Sciences Annual Meeting
2014	American Heart Association Scientific Sessions
2015	International Society for Heart Research annual meeting, Bordeaux, France
2015	American Heart Association Scientific Sessions
2016	American Heart Association Scientific Sessions
2017	American Heart Association Scientific Sessions

2017-2022 American Society for Clinical Investigation Annual Meeting

Leadership Committees:

2005-2015	American Heart Association Council on Basic Cardiovascular Sciences Leadership Committee, Member at large
2004-2006	American Heart Association Council on Basic Cardiovascular Sciences Leadership Committee, representing Early Career Invest.
2013-present	International Society for Heart Research Leadership Council Member
2016-present	American Society for Clinical Investigation Council Member
2017-2019	American Society for Clinical Investigation Secretary-Treasurer
2019	American Society for Clinical Investigation Secretary-Vice President

Major Committees:

2005-2007	Assembly Delegate for National Basic Cardiovascular Sciences to the American Heart Association
2005-2009	Member, American Heart Association Minority Travel Grant Committee
2004-2015	Member, American Heart Association BCVS Leadership Committee
2006-2010	American Heart Association International Mentoring Program
2007-2009	American Heart Association National Speaker Program Education Committee Chair
2007	Early Career Symposium 2007 Program Committee

2007-2008	Member, American Heart Association Members Benefits Task Force
2007-2009	Faculty, American College of Cardiology Clinical Focus Series
2007-2009	Co-Editor, Communications Committee, American Heart Association BCVS Council
2008-2009	Chairperson, American Heart Association CVD Student Scholarship Committee
2008-2013	Chair of the Communications Committee/Newsletter Editor, American Heart Association BCVS Council
2009-2013	The Society of Atherosclerosis Imaging and Prevention (SAIP) Task Force Member
2009-2010 Strategic	Member, American Heart Association Scientific Publishing Planning Committee
2009-2013	Member, American Heart Association Scientific Publishing Committee
2009-2014 Committee	Chair, American Heart Association BCVS Membership Committee
2009-2011 Association	Member, Search Committee for the American Heart Association <i>Hypertension</i> Journal Chief Editor
2009-2011	Member, Search Committee for the Journal of the American Heart Association Chief Editor
2012	Member, American Heart Association Scientific Publishing Committee Editor Review committee
2012	Member, American Heart Association Science Classification Taskforce
2012	Vice Chair, American Heart Association CME Training Program

Taskforce

2012	Member, Task Force on AHA Fellowship Criteria, Council Operations Committee
2013-2016	Chair, American Heart Association CME Journal Training Program Taskforce
2013-present	Member, American Heart Association Open Science Committee
2014-present	Co-Chair, American Society for Clinical Investigation YPSA Meeting Committee
2015	Member, NHLBI AIDS Working Group
2015-present	American Heart Association Council Operations Committee

EDITORIAL RESPONSIBILITIES:

Book Editorial Activity:

Editor, Manual of Cardiovascular Research Techniques. Published by Wiley in 2013

Journal Editorial Activity:

2003-2006 the New	Co-Editor, Johns Hopkins Cardiology News & Issues in Millennium
2010-present	Editorial Board, <i>Circulation Research</i>
2012-present	Editorial Board, <i>PLoS ONE</i>
2013-present	Editorial Board, <i>Journal of the American Heart Association</i>
2015-present	Consulting Editor, <i>JCI Insight</i>
2017-present	Consulting Editor, <i>Circulation Research</i>
2021-present	Board of Reviewing Editors, <i>eLife</i>
2022-present	Deputy Editor, <i>Journal of Clinical Investigation</i>

REVIEWR RESPONSIBILITIES:

Study Sections and Grant Reviews:

2005	German-Israeli-Foundation Young Scientists' Program
2005-2009	American Heart Association Committee on Student Scholarships in CV Disease & Stroke
2006-2009	American Heart Association Minority Travel Grants
2007	American Cancer Society-Institutional Research Grant Review Committee
2009	NIH Challenge Grant Review
2010	Northwestern Rosenberg Grant Review
2010	American Medical Association Research Seed Grant Review
2010	NIH RC4 grant review
2011	Ad-hoc reviewer, CVRS SEP Review, CSR, NIH
2011	NHLBI MAPGen Knowledge Base (MAPGenKB) and Coordination Center and Research Center (U01) Special Emphasis Panel
2011	NIH Director's Early Independence Awards (DP5)
2011	Ad hoc reviewer for NIH/NHLBI Program Project Grant (PPG)
2012-13	Ad hoc reviewer, Stress and Aging, NIA SEPs, NIH
2012	Ad hoc reviewer for Diabetes UK Grants
2010-2016	American Heart Association Basic Cell—Cell Structure and Survival (CSS) 2 Committee
2011-2016	American Society for Advancement of Science International

grant review

2014	Ad-hoc reviewer, CCHF Study section, CSR, NIH
2014	Ad-hoc reviewer, NCI P01 Program Project Meeting II
2014	Ad-hoc reviewer, NIEHS R21/R33 ZES1 LWJ-D (ME) study section
2014-2016	Chair, American Heart Association Basic Cell- Cell Structure and Survival (CSS) 2 Committee
2015	Ad-hoc reviewer,
2015	Ad-hoc reviewer, ZRG1 CVRS-K (02) study section
2015-2019	Member, NIH CCHF study section
2019	Ad-hoc reviewer, NIH HCCS study section

Journal Reviewer:

JAHA

Circulation Research

European Heart Journal

Cell Death & Differentiation

Human Molecular Genetics

Journal of Clinical Investigation

Journal of Experimental Biology

Diabetes

Cell Reports

European Journal of Clinical Investigation

Antioxidants & Redox Signaling (reviewing Editor)

American Journal of Physiology-Heart and Circulatory Physiology
Journal of Molecular and Cellular Cardiology
Circulation: Heart Failure
Frontiers in Drug Metabolism
European Journal of Heart Failure
Journal of American College of Cardiology
Journal of Cellular and Molecular Medicine
American Journal of Physiology-Cell Physiology
Leukemia
Journal of Clinical Oncology
FEBS Journal
Translational research
Seminars in Arthritis and Rheumatism
American Heart Journal
Circulation
Journal of Applied Physiology
Protein Science
Molecular Cancer Therapeutics
International Journal of Cardiology
EMBO reports
IUBMB Reviews
Journal of Clinical Investigation
PLoS One

Science Translational Medicine

Cell Reports

Science Advances

Elife

JCI Insight

GRANT AWARDS

Role: Principal Investigator

Agency: NIH R01 HL155953

Title: "Role of mRNA-binding protein tristetraprolin in cardiac mRNA regulation and the development of heart failure"

Dates: 01/01/2022-12/31/2025

Total Costs: \$2,952,403

Role: Principal Investigator

Agency: 2T32GM008152-31

Title: "Medical Scientist Training Program"

Dates: 07/01/2022 – 06/30/2027

Total Costs: \$7,489,257

Role: Co-Principal Investigator

Agency: K12 HL143959-01

Title: "Third Coast HIV-Related Cardiovascular and Sleep Disorders
K12 Career
Development Program"

Dates: 07/01/2018 – 06/30/2023

Total Costs: \$1,562,233

Role: Principal Investigator

Agency: NIH R01 HL140973-01

Title: "Mechanistic insights into HIV-mediated heart failure with preserved
ejection
fraction"

Dates: 01/01/2018-12/31/2022

Total Costs: \$2,669,478

Role: Principal Investigator

Agency: NIH R01 HL138982-01A1

Title: "Mechanistic insights into the deleterious effects of SIRT2 in the
heart under stress conditions"

Dates: 12/01/2017-11/30/2023

Total Costs: \$2,890,468

Role: Ardehali, Hirsch Co-PI

Agency: Leducq Foundation

Title: "Leducq Transatlantic Network of Excellence -Targeted Approaches for Prevention and Treatment of Anthracycline-Induced Cardiotoxicity"

Dates: 01/01/2021-12/31/2025

Total Costs: \$5,500,000

Role: Principal Investigator

Agency: NIH 1 R01 HL140927-01

Title: "Mechanistic insights into the role of mitochondrial iron in doxorubicin-induced cardiomyopathy using human induced pluripotent stem cells"

Dates: 12/01/2019-11/30/2023

Total Costs: \$1,891,612

Priority Score: \$2,890,468

Completed:

Role: Principal Investigator

Agency: Johns Hopkins Clinical Scientist Award

Title: "Functional Characterization of mABC-1 protein"

Dates: 2004-2006

Total costs: salary support. Was terminated in Dec 2004 after move to Northwestern.

Role: Principal Investigator

Agency: GlaxoSmithKline Grant Award for Young Investigator

Title: "Functional Characterization of the mitochondrial ATP-binding cassette protein-1"

Dates: 2004-2006

Total costs: \$50,000 per year for two years.

Role: Principal Investigator

Agency: Northwestern Memorial Hospital Young Investigator Award

Title: "Role of the mitochondrial ATP-binding cassette protein-1 in protection of the heart against ischemia"

Dates: 2006-2007

Total Costs: \$25,000 for one year

Role: Principal Investigator

Agency: American Cancer Society-Institutional Research Grant

Title: "Role of hexokinase binding to mitochondria in cancer progression"

Dates: 1/2007-1/2008

Total Costs: \$25,000

Role: Principal Investigator

Agency: Schweppe Foundation

Title: "Analysis of the Role of Mitochondrial ATP-Binding Cassette Protein-1 in Cellular Protection"

Dates: 2006-2008

Total Costs: \$50,000 for two years

Role: Principal Investigator

Agency: American Cancer Society-IL Chapter

Title: "Role of hexokinase binding to the mitochondria in cancer growth"

Dates: 1/2007-1/2008

Total Costs: \$98,018

Role: Principal Investigator

Agency: American Heart Association

Title: "Role of hexokinase binding to the mitochondria in myocardial protection"

Dates: 1/1/2007-12/31/2008

Total Costs: \$132,000

Role: Principal Investigator

Agency: NIH K08 HL079387-01

Title: "Functional Characterization of mABC-1 protein"

Dates: 2005-2010

Total costs: \$672,840

Role: Principal Investigator

Agency: The Rosenberg Translational Research Pilot Projects

Title: "A novel approach using microRNA downregulation to inhibit cancer growth"

Dates: 2/1/09-1/31/10

Total Costs: \$75,000

Role: Co-Principal Investigator

Agency: Chicago Biomedical Consortium

Title: "Proteomic analysis of mitochondrial and sarcomeric proteins in cardiomyopathy"

Dates: 2/2008-2/2010

Total Costs: \$33,000

Role: Mentor (PI: Eugene Wyatt)

Agency: American Heart Association

Title: "Regulation of Hexokinase Binding to Mitochondria in the Heart"

Dates: 7/2008-6/2010

Total Costs: \$52,000

Role: Mentor (PI: Rongxue Wu)

Agency: American Heart Association

Title: "Role of the mitochondrial ATP-binding cassette protein-2 in cellular protection"

Dates: 1/2008-12/2010

Total Costs: \$95,224

Role: Principal Investigator

Agency: NIH 1 R01 HL087149-01A1

Title: "Role of the mitochondrial ATP binding cassette protein-1 in cellular protection"

Dates: 6/1/07-5/31/12

Total Costs: \$1,887,500

Role: Principal Investigator

Agency: NIH 1 R01 HL087149-S1

Title: "Role of the mitochondrial ATP binding cassette protein-1 in cellular protection"

Dates: 9/1/09-8/30/11

Total Costs: \$245,007

Role: Mentor (PI: Kannan Mutharasan, MD)

Agency: NIH 1 F32 HL095339-01

Title: "The Role of microRNA-210 in the Hypoxia"

Dates: 1/2009-12/2011

Total Costs: \$174,474

Role: Mentor (PI: Amy Rines)

Agency: American Heart Association

Title: "The role of SNRK in cardiomyocyte metabolism and survival"

Dates: 7/2010-6/2012

Total Costs: \$54,000

Role: Mentor (PI: Marina Bayeva)

Agency: American Heart Association

Title: "Role of mABC1 in mitochondrial biogenesis and DNA damage in the heart"

Dates: 07/2010-06/2012

Total Costs: \$54,000

Role: Mentor (PI: Jimmy Chang)

Agency: American Heart Association

Title: "Role of mitochondrial iron in cardiac response to injury and development of cardiomyopathy"

Dates: 7/2012-6/2014

Total Costs: \$54,000

Role: Principal Investigator

Agency: NIH R01 HL104181-01A1

Title: "The role of microRNA210 in cardiomyocyte response to ischemia-reperfusion"

Dates: 04/01/2011-03/31/2015

Total Costs: \$1,891,612

Role: Principal Investigator for Project 3 (PI of the PPG: Douglas Losordo)

Agency: NIH 1PO1 HL108795-01

Title: "Cardiovascular Regenerative Medicine". Section 3 Title:
"Characterization of mitochondrial defects in EPCs in diabetes and aging."

Dates: 09/07/2011-04/30/2016

Total Costs: \$10,851,457. Costs associated with Section 3: \$1,891,612

Role: Principal Investigator

Agency: NIH 1 K02 HL107448-01

Title: "Mechanistic insights into the cardioprotective effects of mABC1 protein"

Dates: 04/01/2011-05/31/2016

Total Costs: \$504,209

Role: Mentor (PI: Xiaoyan Yang)

Agency: American Heart Association

Title: "Role of sucrose non-fermenting-1 related kinase (SNRK) in cardiac metabolism"

Dates: 7/2014-6/2016

Total Costs: \$112,072

Role: Mentor (PI: Sumeyye Yar)

Agency: American Heart Association

Title: "The role of an mRNA binding protein, tristetraprolin, in the regulation of cardiac branched-chain amino acid catabolism"

Dates: 01/01/2016--12/31/2017

Total Costs: \$112,072

Role: Principal Investigator

Agency: Third Coast CFAR Pilot Award program

Title: "Insights into the mechanism for HIV-related heart failure with preserved ejection fraction"

Dates: 07/01/2016-06/30/2017

Total Costs: \$50,000

Role: Mentor (PI: Konrad Sawicki)

Agency: NIH 1 F30 DK102341-01

Title: "Regulation of metabolism and diabetes mellitus by tristetraprolin"

Dates: 7/2014-6/2018

Total Costs: \$155,805

Role: Co-Investigator

Agency: American Heart Association SFRN

Title: "Phosphate and FGF23: Dietary and Molecular Mediators of Health Disparities in Cardiovascular and Kidney Diseases"

Dates: 07/01/2015-06/30/2019

Role: Mentor (PI: Hidemichi Kouzu)

Agency: American Heart Association

Title: “Role of tristetraprolin in cardiac fatty acid metabolism and development of heart failure”

Dates: 07/2016-06/2018

Total Costs: \$112,072

Role: Mentor (PI: Jason Shapiro)

Agency: NIH 1F30DK109608-01

Title: “The Role of an RNA Binding Protein, Tristetrapolin, in Hepatic Glucose Metabolism and the Development of Diabetes”

Dates: 04/01/2016 - 03/21/2020

Total Costs: \$299,252.00

Role: Principal Investigator

Agency: AHA Grant-in-Aid

Title: "Role of tristetraprolin in cardiac fatty acid metabolism and the development of heart failure”

Dates: 07/01/2017-06/30/2019

Total Costs: \$154,000

Role: Principal Investigator

Agency: NIH R01 HL127646-01A1

Title: "Role of SNRK in cardiac metabolism and development of heart failure”

Dates: 12/01/2015-11/30/2019

Total Costs: \$1,891,612

Role: Mentor (PI: Adam De Jesus)

Agency: NIH 1F31HL132552-01

Title: “Role of tristetraprolin in cardiac mRNA stability and the development of heart disease”
Dates: 04/01/2016 - 03/21/2020
Total Costs: \$299,252.00

INVITED LECTURES:

2003	American Heart Association Basic Cardiovascular Sciences Annual Meeting, Snowbird, UT
2004	29 th Congress of the Federation of European Biochemical Societies. Warsaw, Poland
2005	Biophysical Society Meeting, Long Beach, CA
2005	Northwestern University Pulmonary Medicine Research Conference
2005	University of Illinois Cell Death and Division Meeting
2005	Northwestern University Cardiology Grand Rounds
2005	Keynote Speaker, Northwestern University Medical Scientist Training Program Annual Retreat
2005	University of Illinois Department of Physiology and Biophysics Seminar
2005	Northwestern University Monthly Departmental Research Seminar Series
2006	Central Society for Clinical Research Annual Meeting
2006	University of Illinois Chicago Dept. of Pharmacology Monthly Seminar
2006	Cleveland Clinic Lerner Research Institute Seminar
2007	Chiba University Cardiology Seminar, Japan
2007	Keio University Cardiology Seminar, Japan

2007	Kyoto University Molecular Cardiology Seminar Series, Japan
2007	University of Sapporo Cardiology Seminar Series, Japan
2007	Northwestern University Cardiology Grand Rounds
2007	American Heart Association Young Investigator Forum
2008	University of Chicago Molecular Medicine Series
2008	University of Pisa (Italy) Molecular Cardiology Seminar
2008	Women's & Men's Health Symposium, Munster Hospital
2008	Thorek Hospital (Chicago) Grand Rounds
2008	St. Elizabeth and St. Mary Hospital (Chicago) Grand Rounds
2009	Thorek Hospital (Chicago) Grand Rounds
2009	Central Society for Clinical Research Annual Meeting
2009 Research, Japanese	Keynote speaker, International Society for Heart Section, Sapporo, Japan
2009	Cardiology Grand Rounds, University of Illinois, Chicago
2010	Cardiology Grand Rounds, University of Chicago
2010	Cardiology Grand Rounds, Northwestern University
2010 University	Department of Mol Physiology Seminar Series, Vanderbilt
2010 Southwestern	Division of Cardiology Research Seminar Series, UT
2010 Fredrick	7 th Annual North American ABC Genetic Workshop, NCI-
2011	Cardiology Seminar Series, Mount Siani Hospital, Chicago
2011	Adventist Hospital Grand Rounds, Bollingbrook, IL

2011 IL	Cardiology Grand Rounds, Vista Medical Center, Waukegan,
2011	Adventist Hinsdale Hospital Grand Rounds, Hinsdale, IL
2011 IN	Elkhart General Hospital Cardiology Grand Rounds, Elkhart,
2011 Youngstown, OH	Northside Medical Center Cardiology Seminar Series,
2011 Crest, IL	Advocate South Suburban Cardiology Grand Rounds, Hazel
2011	Northwestern Infectious Diseases Seminar Series
2011	University of Utah Metabolism Group Seminar Series
2011	ABC Annual Meeting, Frederick, Maryland
2011	Boston University Mitochondrial group seminar
2011	University of Minnesota Endocrinology Seminar Series
2012	University of Maryland Cardiology Grand Rounds
2012	University of Wroclaw and Wroclaw Military Hospital Cardiology Conference, Wroclaw, Poland
2012	FEBS ABC2012 Conference invited Speaker, Innsbruck, Austria
2012	Heart Failure Association of the ESC Translational Workshop on Mitochondria & Metabolism, Brussels, Belgium
2012	Loyola University Cell and Molecular Physiology Seminar Series
2012	Annual Congress of the Korean Society of Cardiology National Conference, Busan, South Korea
2012	ABC Annual Meeting, Frederick, Maryland

2012 Belgrade, Serbia	Heart Failure Association of the ESC Annual Meeting,
2013	HFA Annual meeting of the ESC, Les Diablerets, Switzerland
2013	University of Illinois, Chicago Cardiology Grand Rounds
2013	Northwestern University Endocrinology Ground Rounds
2013	Bayer Pharma Conference of Diastolic Heart Failure, Dusseldorf, Germany
2013	American Heart Association Scientific Conference – sessions on: Metabolic Signaling in the Cardiac System Novel Molecular Mechanisms of Mitochondrial Biology in the Heart
2014	Sanofi Mitochondria and Disease Symposium, Boston, MA
2014	Case Western Molecular Cardiology Conference, Cleveland, OH
2014	Northwestern HIV monthly conferences
2014	University of Chicago Cardiology Research Conference
2014	Great Wall International Congress of Cardiology, Beijing, China
2014	Leducq Foundation Mitochondrial group Keynote Speaker, Chicago, IL
2014	Northwestern University Cardiology Grand Rounds
2015	Rutgers University Cardiology Research Conferences
2015	University of Miami Division of Cardiology Conference
2015	San Diego State University Cardiology Research Conferences

2015	Baylor College of Medicine CVRI Conference
2015	Qianjiang International Conference of Cardiology, Hangzhou, China
2016	NYU-Abu Dhabi conference, Abu Dhabi, UAE
2016	ISHR International meeting, Buenos Aires, Argentina
2016	University of South Dakota Division of Basic Biomedical Sciences Seminar Series, Vermillion, South Dakota
2016	University of Cincinnati Heart, Lung and Vascular Institute Seminar Series, Cincinnati, OH
2016	University of Washington Cardiovascular Seminar Series, Seattle, WA
2017	University of California San Diego Cardiovascular Seminar Series, San Diego, CA
2017	University of California San Diego Cardiology Grand Rounds, San Diego, CA
2017	Cedars Sinai Heart Institute Grand Rounds, Los Angeles, CA
2017	Cedars Sinai Cardiovascular seminars, Los Angeles, CA
2017	Columbia University Center For Advanced Cardiac Care Seminar Series, New York, NY
2017	European Society for Cardiology Heart Failure Annual Conference, Paris, France
2017	International Society for Heart Research, North American Section, New Orleans, LA
2017	International Society for Heart Research, European Section, Hamburg, Germany
2017	International BioIron Society Conference, Los Angeles, CA
2017	Qingdao Mencius Lecture, Qingdao, China

2017	American Heart Association BCVS Annual Conference, Portland, OR
2017	Qianjiang International Conference of Cardiology, Hangzhou, China
2017	University of Chicago Cardiovascular Sciences Lecture Series
2017	International Society for Heart Research, Japanese Section
2017	Vanderbilt University Flexner Lecture Series
2017	Henry Ford Hospital Cardiology Grand Rounds
2018	British Heart Foundation/JCI Joint International Symposium, London, England
2018	LSU Malcolm Feist Cardiovascular Disease Seminars
2018	Northwestern University Cardiology Grand Rounds
2018	University of North Carolina-Chapel Hill Cardiovascular Seminar Series
2018	Mount Sinai Icahn School of Medicine Cardiovascular Research Seminar Series
2018	University of Minnesota Lillehei Heart Institute Seminar Series
2018	University of Utah Center for Iron and Heme Disorders Seminar Series
2018	ASPET Annual Meeting at Experimental Biology – San Diego
2018	University of Texas, Houston Brown Foundation Institute of Molecular Medicine Seminar Series
2018	1 st Olympiad in Cardiovascular Medicine - International Symposium on Experimental & Clinical Cardiology – Athens, Greece
2018	The ISHR North American section meeting, Halifax, CA
2018	University of Alabama CV Research Seminar Series

2018	University of Padova Distinguished Lecture Series, Padova, Italy
2018	University of Torino Cardiovascular Research Seminar, Torino, Italy
2018	USA-China Cardiovascular Symposium & China Night, Chicago, IL
2018	University of Utah Cardiology Grand Rounds
2019	Washington University Center for Cardiovascular Research Seminar Series
2019 Honolulu, HI	3 rd New Frontiers in Cell Death Signaling and Heart Failure,
2019 Seminar Series	University of Manitoba Institute of Cardiovascular Sciences
2019 Series	University of Minnesota Cardiovascular Research Seminar
2019	University of Kansas Department of Cardiovascular Medicine Seminar
2019	International BioIron Society Conference, Heidelberg, Germany
2019	Cardiology Grand Rounds, Medical College of Wisconsin
2019	International Society for Heart Research, Beijing, China
2019	Qianjiang International Conference of Cardiology, Hangzhou, China
2020	Mount Sinai Monthly Cardiology Conference, Virtual
2020	4 th New Frontiers in Cell Death Signaling and Heart Failure, Honolulu, HI
2020	Tel Aviv University Symposium on Biomed Research, Tel Aviv, Israel
2020	International Society for Heart Research European Section, Virtual

2020	Qianjiang International Conference of Cardiology, Hangzhou, China
2021	International Society for Heart Research Japanese Section, Keynote speaker
2021	International Society for Heart Research North American Section, Denver, CO
2022	5 th New Frontiers in Cell Death Signaling and Heart Failure, Honolulu, HI
2022	Association of Physicians Annual Conference, Dublin, Ireland
2022	American Society for Clinical Investigation, Presidential Address
2022	Columbia University Cardiovascular Research Conference
2022	second Olympiad of Cardiovascular Research, Crete, Greece
2022	International Society for Heart Research, Berlin, Germany
2022	International Society for Heart Association, North American Section, Winnipeg, Canada
2022	Japanese Heart Failure Society, Hiroshima, Japan
2023	New Frontiers in Cell Death Signaling and Heart Failure, Honolulu, HI
2023	INSERM cardiotoxicity Conference, Paris, France
2023	Association of Physicians, Liverpool, England
2023	CVBE2023 conference, Kyoto, Japan
2023	International BioIron conference, Plenary talk, Darwin, Australia

PUBLICATIONS

A. Original Investigation/Reviews/Editorials

1. Printz RL, **Ardehali H**, Koch S, Granner DK. Human hexokinase II mRNA and gene structure. *Diabetes*. 44: 290-294. 1995.
2. **Ardehali H.**, Printz, R, Koch S, Phillips J, Granner DK. Isolation, Characterization, and chromosomal localization of a human pseudogene for hexokinase II. *Gene*. 164: 357-361. 1995.
3. **Ardehali H**, Yano Y, Printz RL, Koch S, Whitesell RR, May JM, Granner DK. Functional organization of mammalian hexokinase II: retention of catalytic and regulatory functions in both the amino- and carboxy-terminal halves. *J. Biol. Chem*. 271: 1849-1852. 1996.
4. **Ardehali H**, Tiller GE, Printz RL, Mochizuki H, Prochazka M, Granner DK. A novel (TA)_n polymorphism in the hexokinase II gene: application to non-insulin-dependent diabetes mellitus in the Pima Indians. *Human Genetics*. 97: 482-485. 1996.
5. Printz RL, Osawa H, **Ardehali H**, Koch S, Granner DK. Hexokinase II gene: structure, regulation and promoter organization. *Biochem Society Transactions*. 25: 107-112. 1997.
6. Voget C, Yki-Jarvinen H, Iozzo P, Pendergrass M, Koval J, **Ardehali H**, Printz R, Granner D, DeFronzo R, Mandarino L. Effects of Insulin on subcellular localization of hexokinase II in human skeletal muscle *in vivo*. *J. Clin. Endocrinol. Metab*. 83: 230-234. 1997.
7. Pendergrass M, Koval J, Voget C, Yki-Jarvinen H, Iozzo P, Pipek R, **Ardehali H**, Printz R, Granner D, DeFronzo R, Mandarino L. Insulin-induced hexokinase II expression is reduced in obesity and NIDDM. *Diabetes*. 47: 387-394. 1997.
8. Koval J, DeFronzo R, O'Doherty R, Printz R, **Ardehali H.**, Granner D,

Mandarino L. Regulation of hexokinase II activity and expression in human muscle by moderate exercise. *American J. Physiol.* 274: E304-308. 1997.

9. **Ardehali H**, Printz RL, Whitesell RR, May JM, Granner DK. Functional interaction between the N- and C-terminal halves of human hexokinase II. *J. Biol. Chem.* 274: 15986-15989. 1999.
10. Voget C, **Ardehali H**, Iozzo P, Yki-Jarvinen H, Koval H, Maezono K, Pendergrass M, Printz R, Granner D, DeFronzo R, Mandarin, L. Regulation of hexokinase II expression in human skeletal muscle in vivo. *Metabolism* 49(6): 814-818. 2000.
11. **Ardehali H**, Buetens O, Garcia DA. Thoracic actinomycosis and liver abscesses. *Osler Medical Journal*. Winter 2000.
12. Cusi KJ, Pratipanawatr T, Koval J, Printz R, **Ardehali H**, Granner DK., DeFronzo RA, Mandarino LJ. Exercise increases hexokinase II mRNA, but not activity in obesity and type 2 diabetes. *Metabolism*. 50(5): 602-606. 2001.
13. **Ardehali H**, Volmar K, Roberts C, Forman M, Becker L. Fatal disseminated adenoviral infection in a renal transplant patient. *Transplantation*. 71: 998-999. 2001.
14. **Ardehali H**, Kasper E, Baughman K. Peripartum cardiomyopathy. *Minerva Cardioangiologica* 51(1): 41-48. 2003.
15. Whitesell RR, **Ardehali H**, Printz RL, Beechem J, Knobel SM, Piston DW, Granner DK, Van Der Meer W, Perriott L, May JM. Control of glucose phosphorylation in L6 myotubes by compartmentalization, hexokinase and glucose transport. *Biochem. J.* 370(Pt 1):47-56. 2003.
16. **Ardehali, H.**, Farb, A., Brown, C., Schulman, S. Acute thrombosis of a separate major coronary artery during initially successful thrombolytic therapy. *Int. J. Cardiol.* 89(1): 97-9. 2003.

17. **Ardehali H**, Qasim A, Cappola T, Howard D, Hruban R, Hare J, Baughman KL, Kasper KK. Endomyocardial biopsy plays a major role in diagnosing patients with unexplained cardiomyopathy. *Am. Heart J.* 147(5): 919-23. 2004.
18. **Ardehali H**. 2004. Mitochondrial ATP-sensitive K⁺ channel and cardioprotection. *Acta Biochimica Polonica* 51(2): 379-390.
19. **Ardehali H.**, Chen Z, Ko Y, Mejia-Alvarez R, Marbán E. Multiprotein complex containing succinate dehydrogenase confers mitochondrial ATP-sensitive K⁺ channel activity. *PNAS* 101(32): 11880-5. 2004.
20. Whitesell RR, **Ardehali H**, Beechem JM, Powers AC, Van Der Meer W, Periot LM, Granner DK Compartmentalization of transport and phosphorylation of glucose in a hepatoma cell line. *Biochem J.* 386(Pt 2):245-53. 2004.
21. **Ardehali H**, Kasper E, Baughman K. Approach to the patient with cardiomyopathy: Whom to biopsy. *Am. Heart J.* 149(1): 7-12. 2005.
22. **Ardehali H**, O'Rourke B. Mitochondrial K_{ATP} channels in cell survival and death. *J. Mol. Cell. Cardiology* 39(1):7-16. 2005.
23. **Ardehali H**. Cytoprotective channels in mitochondria. *J. Bioenerg. Biomembr.* 37(3):171-7. 2005.
24. **Ardehali H**, Howard D, Hariri R, Qasim A, Hare J, Baughman KL, Kasper KK. A positive endomyocardial biopsy result for sarcoid is associated with poor prognosis in patients with initially unexplained cardiomyopathy. *Am. Heart J.* 150(3):459-63. 2005.
25. **Ardehali H**, O'Rourke B, Marban E. Cardioprotective role of the mitochondrial ATP-binding cassette protein-1. *Circulation Research* 97(8):740-2. 2005.

26. **Ardehali H**, Xue T, Dong P, Macahmer C. Targeting of the mitochondrial membrane proteins to the cell surface for functional studies. *Biochem Biophys Res Commun*. 338(2):1143-51. 2005.
27. Michos ED, Ardehali R, Blumenthal R, **Ardehali H**. Aspirin and clopidogrel resistance: A review. *Mayo Clinic Proceedings*. 81(4):518-26. 2005.
28. Bowers M, **Ardehali H**. TOM20 and the Heartbreakers: evidence for the role of mitochondrial transport proteins in cardioprotection. *J. Mol. Cell Card*. 41(3):406-9. 2006.
29. **Ardehali H**. Signaling mechanisms in ischemic preconditioning: Interaction of PKC ϵ and MitoK_{ATP} in the inner membrane of mitochondria. *Circulation Research* 99:798-800. 2006.
30. Burke, MA, **Ardehali H**. Mitochondrial ATP-binding cassette proteins. *Transl Res* 150(2):73-80. 2007.
31. Leyngold I, Baughman K, Kasper E, **Ardehali H**. Comparison of survival among patients with connective tissue disease and cardiomyopathy (systemic sclerosis, systemic lupus erythematosus, and undifferentiated disease). *Am J Cardiol*. 100(3):513-7. 2007.
32. Sun L, Shukair S, Naik TJ, Moazed F, **Ardehali H**. Glucose phosphorylation and mitochondrial binding are required for the protective effects of hexokinase I and II. *Mol. Cell. Biol*. 28(3):1007-17. 2008.
33. Burke MA, Mutharasan RK, **Ardehali H**. The sulfonylurea receptor, an atypical ATP-binding cassette protein, and its regulation of the KATP channel. *Circ Research* 102(2):164-76. 2008.
34. Gordon L, Singh A, Prachand S, Lieberman E, Sun L, Burke MA, Naik TJ,

Prasad S, **Ardehali H**. Blockade of the erbB2 Receptor Induces Cardiomyocyte Death through Mitochondrial and Reactive Oxygen Species-dependent Pathways. *J. Biol Chem*, 284(4):2080-7. 2008.

35. Decker RS, Rines AK, Nakamura S, Naik TJ, Wassertsrom JA, **Ardehali H**. Phosphorylation of contractile proteins in response to alpha- and beta-adrenergic stimulation in neonatal cardiomyocytes. *Transl Res*. 155(1):27-34. 2010.
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37. Bayeva M, **Ardehali H**. Mitochondrial dysfunction and oxidative damage to sarcomeric proteins. *Current Hypertension Reports*. 12(6): 426-32. 2010.
38. Wu R, Smeele KM, Wyatt E, Ichikawa Y, Eerbeek O, Sun L, Chawla K, Hollmann MW, Nagpal V, Heikkinen S, Laakso M, Jujo K, Wasserstrom JA, Zuurbier CJ, **Ardehali H**. Reduction in hexokinase II levels results in decreased cardiac function and altered remodeling after ischemia/reperfusion injury. *Circulation Research*. 108(1): 60-9. 2010.
39. Wyatt E, Wu R, Rabeh W, Park H-W, Ghanefar M, **Ardehali H**. Regulation and cytoprotective role of hexokinase III. *PLoS ONE*. 5(11):e13823. 2010.
40. Sarma S, **Ardehali H**, Gheorghiade M. Enhancing the metabolic substrate: PPAR-alpha agonists in heart failure. *Heart Failure Reviews*. 14(2):120-9. 2010.
41. McMahon KM, Mutharasan RK, Tripathy S, Veliceasa D, Bobeica M, Shumaker DK, Luthi AJ, Helfand BT, **Ardehali H**, Mirkin CA, Volpert O, Thaxton CS. Biomimetic High Density Lipoprotein Nanoparticles For Nucleic Acid Delivery. *Nano Lett*. 11(3):1208-14. 2011.

42. Smeele KM, Southworth R, Wu R, Xie C, Nederlof R, Warley A, Nelson JK, van Horssen P, van den Wijngaard JP, Heikkinen S, Laakso M, Koeman A, Siebes M, Eerbeek O, Akar FG, **Ardehali H**, Hollmann MW, Zuurbier CJ. Disruption of Hexokinase II-Mitochondrial Binding Blocks Ischemic Preconditioning and Causes Rapid Cardiac Necrosis. *Circulation Research*. 108(10):1165-9. 2011.
43. Mutharasan RK, Ichikawa Y, **Ardehali H**. microRNA-210 is Upregulated in Hypoxic Cardiomyocytes through Akt- and p53-dependent Pathways and Exerts Cytoprotective Effects. *Am. J. Physiol*. 301(4):H1519-30. 2011.
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45. Wu R, Wyatt E, Chawla K, Tran M, Ghanefar M, Laakso M, Epting CL, **Ardehali H**. Hexokinase II knockdown results in exaggerated cardiac hypertrophy via increased ROS production. *EMBO Mol Medicine*. 4, 633–646. 2012.
46. Ichikawa Y, Bayeva M, Ghanefar M, Potini V, Sun L, Mutharasan RK, Wu R, Khechaduri A, Jairaj Naik T, **Ardehali H**. Disruption of ABCB8 in mice leads to cardiomyopathy through a decrease in mitochondrial iron export. *Proc Natl Acad Sci U S A*. 109(11):4152-7. 2012.
This paper was highlighted in *Nature Chemical Biology*.
47. Rines AK, **Ardehali H**. Transition metals and mitochondrial metabolism in the heart. *J Mol Cell Cardiol*. 55:50-7. 2012.
48. Rines AK, Bayeva M, **Ardehali H**. A new pROM-King for the mitoK_{ATP} dance: ROMK takes the lead. *Circulation Research*. 111(4):392-3. 2012.
49. Rines AK, Burke MA, Fernandez R, Volpert O, **Ardehali H**. Snf1-related kinase inhibits colon cancer cell proliferation through calcyclin binding protein-

dependent reduction of β -catenin. *FASEB J.* 26(11):4685-95. 2012.

50. Bayeva M, Khechaduri A, Puig S, Chang HC, Patial S, Blackshear PJ, **Ardehali H.** mTOR Regulates Cellular Iron Homeostasis through Tristetraprolin. *Cell Metabolism.* 16(5):645-57. 2012.

This paper was featured on the cover of *Cell Metabolism*.

51. Marcovina SM, Sirtori C, Peracino A, Gheorghiade M, Borum P, Remuzzi G, **Ardehali H.** Translating the basic knowledge of mitochondrial functions to metabolic therapy: role of L-carnitine. *Transl Res.* 161(2):73-84. 2012.

52. Jankowska EA, Malyszko J, **Ardehali H**, Koc-Zorawska E, Banasiak W, von Haehling S, Macdougall IC, Weiss G, McMurray JJ, Anker SD, Gheorghiade M, Ponikowski P. Iron status in patients with chronic heart failure. *Eur Heart J.* 34(11):827-34. 2013.

53. Bayeva M, Gheorghiade M, **Ardehali H.** Mitochondria as a Therapeutic Target in Heart Failure. *JACC.* 12;61(6):599-610. 2013.

54. Khechaduri A, Bayeva M, Chang, HC, **Ardehali H.** Heme Levels are increased in human failing hearts. *JACC.* 7;61(18):1884-93. 2013.

55. Qiao A, Mutharasan RK, Wu R, **Ardehali H.** microRNA-210 decreases heme levels by targeting ferrochelatase in cardiomyocytes. *J Am Heart Assoc.* 2(2):e000121. 2013.

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61. Bayeva M, Sawicki KT, **Ardehali H**. Taking diabetes to heart--deregulation of myocardial lipid metabolism in diabetic cardiomyopathy. *J Am Heart Assoc*. 2(6):e000433. 2013.
62. Ichikawa Y, Ghanefar M, Bayeva M, Wu R, Khechaduri A, Prasad SV, Mutharasan RK, Naik TJ, **Ardehali H**. Cardiotoxicity of doxorubicin is mediated through mitochondrial iron accumulation. *J Clin Invest*. 124(2):617-30. 2014.
63. Hohl M, **Ardehali H**, Azuaje FJ, Breckenridge RA, Doehner W, Eaton P, Ehret GB, Fujita T, Gaetani R, Giacca M, Hasenfuß G, Heymans S, Leite-Moreira AF, Linke WA, Linz D, Lyon A, Mamas MA, Orešič M, Papp Z, Pedrazzini T, Piepoli M, Prosser B, Rizzuto R, Tarone G, Tian R, van Craenenbroeck E, van Rooij E, Wai T, Weiss G, Maack C. Meeting highlights from the 2013

European Society of Cardiology Heart Failure Association Winter Meeting on Translational Heart Failure Research. *Eur J Heart Fail.* 16(1):6-14. 2014.

64. **Ardehali, H.** How to write a successful grant application and research paper. *Circulation Research.* 114(8):1231-4. 2014.
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B. Book Chapters:

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2. **Ardehali, H.**, Nueremberger, E. Urinary Tract Infections. In: Cheng, A., Zaas, A., ed. The Osler Manual. 2003. Saint Louis: Mosby.
3. **Ardehali, H.** Stable Angina. In: Cardiology...*In a Page*. Edited by Scott Kahan

and Rajnish Prasad 2006, Blackwell Science.

4. **Ardehali, H.** Complications of Myocardial Infarction. In: Cardiology...*In a Page*. Edited by Scott Kahan and Rajnish Prasad 2006, Blackwell Science.
5. **Ardehali, H.** Coronary Artery Disease. In: Cardiology...*In a Page*. Edited by Scott Kahan and Rajnish Prasad 2006, Blackwell Science.
6. **Ardehali, H.** Cardiac Manifestations of Systemic Disease: SLE. In: Cardiology...*In a Page*. Edited by Scott Kahan and Rajnish Prasad 2006, Blackwell Science.
7. **Ardehali, H.** Diastolic Heart Failure. In: Cardiology...*In a Page*. Edited by Scott Kahan and Rajnish Prasad 2006, Blackwell Science.

Appendix B

Exhibit	Description
2002	Australia New Zealand Clinical Trials Registry, The LoDoCo Trial: The effect of low dose colchicine on the natural history of patients with stable coronary artery disease (ACTRN12610000293066) (2014) (“LoDoCo Trial”)
2003	Clinicaltrials.gov identifier NCT01327846, <i>Cardiovascular Risk Reduction Study (Reduction in Recurrent Major CV Disease Events) (CANTOS)</i> , https://clinicaltrials.gov/study/NCT01327846?titles=CANTOS&rank=1 (last accessed Oct. 4, 2023) (“CANTOS”)
2004	Clinicaltrials.gov identifier NCT02551094, <i>Colchicine Cardiovascular Outcomes Trial (COLCOT)</i> , https://clinicaltrials.gov/study/NCT02551094?titles=COLCOT&rank=1 (last accessed Oct. 4, 2023) (“COLCOT”)
2005	M. Imazio et al., <i>Colchicine in addition to conventional therapy for acute pericarditis: results of the Colchicine for acute Pericarditis (COPE) trial</i> , 112 CIRCULATION 2012-2016 (2005) (“Imazio 2005a”)
2006	M. Imazio et al., <i>Colchicine as first choice therapy for recurrent pericarditis: results of the CORE (Colchicine for Recurrent pericarditis) trial</i> , 165 ARCH. INTERN. MED. 1987-1991 (2005) (“Imazio 2005b”)
2007	M. Imazio et al., <i>Colchicine for recurrent pericarditis (CORP): a randomized trial</i> , 155 ANN. INTERN. MED. 409-414 (2011) (“Imazio 2011”)
2008	Maria Isabel Lopes et al., <i>Beneficial effects of colchicine for moderate to severe COVID-19: a randomized, double-blinded, placebo-controlled clinical trial</i> , 7 RMD Open 1455 (2021)
2009	J.H. O’Keefe et al., <i>Ineffectiveness of colchicine for the prevention of restenosis after coronary angioplasty</i> , 19 J. AM. COLL. CARDIOL. 1597-1600 (1992) (“O’Keefe”)
2010	Terkeltaub et al., <i>High versus low dosing of oral colchicine for early acute gout flare: Twenty-four hour outcome of the first multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-comparison colchicine study</i> , 62 ARTHRITIS & RHEUMATOLOGY 1060-1068 (2010)
2011	Declaration of Jean-Claude Tardif, M.D.