## BIOGRAPHICAL SKETCH

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NAME: Antonio Abbate

eRA COMMONS USER NAME (credential, e.g., agency login): AABBATE

POSITION TITLE: '*Ruth C. Heede*' Professor of Cardiology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| University Campus Bio-Medico, Rome, Italy | M.D. | 07/2000 | Medical School |
| Catholic University, Rome, Italy | | 06/2004 | Cardiology |
| Virginia Commonwealth University, Richmond, VA | | 04/2007 | Internal Medicine |
| Catholic University, Rome, Italy | Ph.D. | 03/2009 | Cellular & Molecular Cardiology |

### A. Personal Statement

I am a physician-scientist and a clinical cardiologist by training. I led a translational research team in the Pauley Heart Center, Virginia Commonwealth University, between 2007-2022, and as of July 2022, I am a Resident Faculty in the Robert M. Berne Cardiovascular Research Center and a Clinician in the Division of Cardiology with a dedicated clinic focused on Cardiac Immunology and Oncology at the University of Virginia, and as January 2023 also as Medical Director of the Exercise Physiology Core Lab. I also maintain an external affiliate appointment as Clinical Professor in the Department of Internal Medicine at Virginia Commonwealth University.

As researcher and scientist, my team studies cardiac physiology and drug development, supported by funds from the NIH, AHA and Industry partnerships. My research program is currently funded by a R01 grant titled 'Unconventional IL-1 signaling in heart failure', a R01 clinic grant titled "Prevention of heart failure with IL-1 blockade: a mechanistic study", a R61/R33 grant titled 'IL-1 blockade in recently decompensated heart failure' and a R21 grant titled 'Safety and feasibility of IL-1 blockade in cardiac sarcoiodosis', as well as by industry sponsored studies on ST-segment elevation and heart failure. We have tested several anti-inflammatory drugs in models of heart disease, several of which (Anakinra, Rilonacept, Canakinumab, Prolastin C, SP16, and Dapansutrile) are now in phase I-III clinical trials or FDA-approved for clinical use. Our team has also developed several patents on anti-inflammatory drugs in heart disease (US9522179 B2; PCT/US2011/027283; PCT/US2014/038913-WO2014/190015A1).

*Selected ongoing projects that I would like to highlight for this proposal:*

R61/R33HL139943
**National Heart Lung and Blood Institute / National Institute of Health**
Abbate/Van Tassell (MPI)
07/1/2018-06/30/2023
The effects of Interleukin-1 blockade on exercise capacity in patients with recently decompensated systolic heart failure

R01AG076360
**National Institute of Aging / National Institute of Health**
Abbate/Van Tassell (MPI)
02/22/2022-02/21/2027
Prevention of heart failure with IL-1 blockade: a mechanistic study

R01HL150115
**National Heart Lung and Blood Institute / National Institute of Health**
Abbate/Toldo (MPI)
02/01/2020-01/31/2025
Unconventional Interleukin-1 signaling in heart failure

*Selected Reviews highlighting my expertise in Inflammation, Myocardial Infarction and Heart Failure:*

1. Van Tassell BW, Toldo S, Mezzaroma E, **Abbate A**. Targeting Interleukin-1 in heart disease. ***Circulation***. 2013;128:1910-1923. doi: 10.1161/CIRCULATIONAHA.113.003199. Review. PubMed PMID: 24146121; PubMed Central PMCID: PMC3938092.
2. Seropian IM, Toldo S, Van Tassell BW, **Abbate A**. Anti-inflammatory strategies for cardiac remodeling after ST-elevation acute myocardial infarction. ***J Am Coll Cardiol*** 2014;63:1593-1603. doi: 10.1016/ j.jacc.2014.01.014. Epub 2014 Feb 13. Review. PubMed PMID: 24530674.
3. **Abbate A**, Toldo S, Marchetti C, Kron J, Van Tassell BW, Dinarello CA. Interleukin-1 and the Inflammasome as Therapeutic Targets in Cardiovascular Disease. ***Circ Res***. 2020 Apr 24;126(9):1260-1280. doi: 10.1161/CIRCRESAHA.120.315937. Epub 2020 Apr 23. PMID: 32324502; PMCID: PMC8760628.
4. Toldo S, **Abbate A**. The role of the NLRP3 inflammasome and pyroptosis in cardiovascular diseases. ***Nat Rev Cardiol***. 2024 Apr;21(4):219-237. doi: 10.1038/s41569-023-00946-3. Epub 2023 Nov 3. PMID: 37923829.

## B. Positions and Honors

**Clinical Licensure and Specialty Board Certification**

| | |
|---|---|
| 2021-present | Certification in Cardio-Oncology, International Cardio-Oncology Society |
| 2016-present | Certification in Cardiovascular Medicine, American Board of Internal Medicine |
| 2007-present | Certification in Internal Medicine, American Board of Internal Medicine |
| 2007-present | European Board for the Specialty of Cardiology |
| 2006-present | Unrestricted License for the Practice of Medicine, Virginia Board of Medicine |
| 2001-present | Unrestricted License for the Practice of Medicine, Italian Board of Medicine |

**Positions and Employment**

| | |
|---|---|
| 1/2023-present | Medical Director, Exercise Physiology Core Lab, University of Virginia, Charlottesville, VA. |
| 7/2022-present | Ruth C. Heede Professor of Cardiovascular Medicine, University of Virginia, Charlottesville, VA. |
| 7/2022-present | Resident Faculty Member, Robert M. Berne Cardiovascular Research Center, and Clinical Professor, Department of Internal Medicine, University of Virginia, Charlottesville, VA. |
| 7/2020-6/2022 | Professor of Medicine with tenure, Department of Internal Medicine, Division of Cardiology, Virginia Commonwealth University, Richmond, VA. |
| 5/2018-6/2022 | Associate Director, Center for Clinical and Translational Research – Research Capacity Core Hub Director, Virginia Commonwealth University, Richmond, VA. |
| 5/2015-6/2022 | Medical Director of the Clinical Research Service Unit, Center for Clinical and Translational Research, Virginia Commonwealth University, Richmond, VA. |
| 7/2016-9/2020 | Associate Chair for Research, Department of Internal Medicine, Virginia Commonwealth University, Richmond, VA. |
| 10/2014-9/2020 | Vice-Chair, Division of Cardiology, Virginia Commonwealth University, Richmond, VA. |
| 12/2015-6/2020 | Associate Director of Translational Research, Johnson Center for Critical Care and Pulmonary Research, Virginia Commonwealth University, Richmond, VA. |
| 10/2013-6/2022 | '*James C. Roberts, Esq.*' Professor of Cardiology, Department of Internal Medicine, Division of Cardiology, Virginia Commonwealth University, Richmond, VA. |
| 7/2013-6/2020 | Associate Professor of Medicine (*with tenure*), Department of Internal Medicine, Division of Cardiology, Virginia Commonwealth University, Richmond, VA. |
| 12/2013-8/2015 | Medical Director, Cardiac Rehabilitation Program, Virginia Commonwealth University. |
| 4/2007-6/2013 | Assistant Professor of Medicine, Department of Internal Medicine, Division of Cardiology, Virginia Commonwealth University, Richmond, VA. |
| 4/2007-6/2013 | Associate Program Director, Internal Medicine Training Program, Physician Scientist Track, Virginia Commonwealth University, Richmond, VA. |
| 7/2011-3/2012 | Director, Cardiac Intensive Care Unit, Virginia Commonwealth University |

**Memberships** *(selected)*

| | |
|---|---|
| 2019-present | American College of Cardiology (Fellow ACC since 2019) |
| 2005-present | American Heart Association - Basic Science Council (Fellow AHA since 2019) |
| 2004-present | European Society of Cardiology (Fellow ESC since 2007) |
| 2002-present | Italian Society of Cardiology |

**Honors and Awards** *(selected)*

| | |
|---|---|
| 2024- | Board Member, American Heart Association Eastern States |
| 2020-2024 | Member of NIH Heart, Lung, and Blood Program Project Review Committee |
| 2019 | *Thames-Kontos* Mentoring Award (*Inaugural*) – VCU School of Medicine |
| 2019 | Undergraduate Research Opportunity Program Distinguished Mentor – VCU |
| 2018, 2019 | Immunology Study Group – Chair - American Heart Association |
| 2017 | *Forbes* – Cardiologists Honor Roll – 27 Top Cardiologists |
| 2016, 2017 | Virginia Commonwealth University Excellence in Teaching Award |
| 2016 | Virginia Commonwealth University – School of Medicine – Distinguished Mentor Award |
| 2014-2015 | Cardiac Biology Regulation Study Group – Co-Chair - American Heart Association |
| 2013 | Virginia Commonwealth University Physician Champion Award |
| 2007-2009, 2012 | Virginia Commonwealth University Excellence in Teaching Award |

## C. Contributions to Science

### 1. Interleukin-1 in acute myocardial infarction and failure

I have been working on the role of Interleukin-1 (IL-1) in heart disease all my career, since a medical student. IL-1 has progressed from being an inflammatory biomarker in AMI and heart failure to becoming a key mechanism in the pathophysiology in heart disease in experimental preclinical studies, and finally a therapeutic target for phase II-III clinical trials. This research has been supported by an American Heart Association Scientist Development Award, and National Heart Lung and Blood Instititute R34 and R61/R33 grants, and now a R01 award from the National Institute of Aging.

*Selected publications related to this topic:*

a) **Abbate A**, Salloum FN, Vecile E, Das A, Hoke NN, Straino S, Biondi-Zoccai G, Houser J, Qureshi I, Ownby E, Gustini E, Biasucci LM, Severino A, Capogrossi MC, Vetrovec GW, Crea F, Baldi A,. Kukreja RC, Dobrina A. Anakinra, a recombinant human interleukin-1 receptor antagonist, inhibits apoptosis in experimental acute myocardial infarction. ***Circulation***. 2008 May 20; 117(20): 2670- 83. PMID: 18474815.

b) **Abbate A**, Van Tassell BW, Biondi-Zoccai GG, Kontos MC, Grizzard JD, Spillman DW, Oddi C, Roberts CS, Melchior RD, Mueller GH, Abouzaki NA, Rengel LR, Varma A, Gambill ML, Falcao RA, Voelkel NF, Dinarello CA, Vetrovec GW. Effects of Interleukin-1 Blockade with Anakinra on Adverse Cardiac Remodeling and Heart Failure Following Acute Myocardial Infarction (from the VCU-ART2 Pilot Study). ***Am J Cardiol*** 2013;111:1394-1400. PMID:20451681.

c) Van Tassell BW, Canada J, Carbone S, Trankle C, Buckley L, Oddi Erdle C, Abouzaki NA, Dixon D, Kadariya D, Christopher S, Schatz A, Regan J, Viscusi M, Del Buono M, Melchior R, Mankad P, Lu J, Sculthorpe R, Biondi-Zoccai G, Lesnefsky E, Arena R, **Abbate A**. Interleukin-1 Blockade in Recently Decompensated Systolic Heart Failure: Results From REDHART (Recently Decompensated Heart Failure Anakinra Response Trial). ***Circ Heart Fail*** 2017;10. pii: e004373. doi:10.1161/CIRCHEARTFAILURE.117.004373. PubMed PMID: 29141858; PubMed Central PMCID: PMC5699505.

d) **Abbate A**, Trankle CR, Buckley L, Lipinski MJ, Appleton D, Kadariya D, Canada JM, Carbone S, Roberts CS, Abouzaki N, Melchior R, Christopher S, Turlington J, Mueller G, Garnett J, Thomas C, Markley R, Wohlford G, Puckett L,Medina de Chazal H, Chiabrando JG, Bressi E, Del Buono MG, Schatz A, Vo C, Dixon DL, Biondi-Zoccai GG, Kontos MC, Van Tassell BW. Interleukin-1 blockade Inhibits the Acute Inflammatory Response in Patients with ST-segment Elevation Myocardial Infarction. ***J Am Heart Assoc*** 2020;9(5):e014941. doi:10.1161/JAHA.119.014941. PMID: 32122219.PMCID: PMC7335541.

### 2. Role of the inflammasome in acute myocardial infarction and heart failure

The inflammasome was identified in 2000 as a macromolecular machinery that functions as a ‘sensor of danger’ and ‘factory of pro-inflammatory cytokines’. We were the first to describe the formation of the inflammasome in cardiomyocytes *in vitro* and *in vivo*. We identified the central role of the inflammasome in causing further injury and the first to conduct a phase IB clinical trial in patients with heart failure. This research has been supported by an American Heart Association Beginning Grant-in-Aing, and a National Heart Lung and Blood Instititute R01 grant.

*Selected publications related to this topic:*

a) Mezzaroma E*, Toldo S*, Farkas D, Seropian IM, Van Tassell BW, Salloum FN, Kannan HR, Menna AC, Voelkel NF, **Abbate A**. The inflammasome promotes adverse cardiac remodeling following acute myocardial infarction in the mouse. ***Proc Natl Acad Sci U S A*** 2011;108:19725-30.

b) Toldo S, Mezzaroma E, McGeough MD, Pena CA, Marchetti C, Sonnino C, Van Tassell BW, Salloum FN, Voelkel NF, Hoffman HM, **Abbate A**. Independent roles of the priming and the triggering of the NLRP3 inflammasome in the heart. ***Cardiovasc Res*** 2015;105:203-12. Doi:10.1093/cvr/cvu259. Epub 2014 Dec 18. PubMed PMID: 25524927; PubMed Central PMCID: MC4357795.

c) Toldo S, Marchetti C, Mauro AG, Chojnacki J, Mezzaroma E, Carbone S, Zhang S, Van Tassell B, Salloum FN, **Abbate A**. Inhibition of the NLRP3 inflammasome limits the inflammatory injury following myocardial ischemia-reperfusion in the mouse. ***Int J Cardiol***. 2016 Apr 15;209:215-20. doi: 10.1016/j.ijcard.2016.02.043. Epub 2016 Feb 4. PubMed PMID: 26896627.

d) Wolhford GF, Van Tassell BW, Billingsley HE, Kadariya D, Canada JM, Carbone S, Mihalick VL, Bonaventura A, Vecchiè A, Chiabrando JG, Bressi E, Thomas G, Ho A-C, Marawan AA, Dell M, Trankle CR, Turlington J, Markley R, **Abbate A**. Phase 1B, randomized, double-blinded, dose escalation, single-center, repeated dose safety and pharmacodynamics study of oral NLRP3 inhibitor Dapansutrile in subjects with NYHA II-III systolic heart failure. ***J Cardiovasc Pharmacol*** 2020;77:49-60. PMID: 33235030, PMCID: PMC7774821.

**3. LRP1 as new therapeutic target in acute myocardial infarction and heart failure**

Over the past 10 years, we explored the anti-inflammatory and cardioprotective signals of serine protease inhibitors (SERPINs) and the signaling through the Low-Density Cholesterol Lipoprotein Related Protein 1 (LRP1). Alpha-1 antitrypsin is the prototypical SERPIN, shown to inhibit IL-1 signaling and to promote cell survival. Using a mouse model of acute myocardial infarction, we showed that AAT reduces infarct size, independently of the effects on elastase, and through a LRP1 dependent signal. We showed that a selective LRP1 agonist, SP16, reproduced the benefit of AAT. We also completed a pilot phase I/II clinical trial with plasma derived AAT in patients with STEMI, and a phase I study in healthy volunteers with SP16. This research has been supported by a National Heart Lung and Blood Instititute R56 and R01 grants as well as by an investigator-initiated industry sponsored grant.

*Selected publications related to this topic:*

a) Toldo S, Seropian IM, Mezzaroma E, Van Tassell BW, Salloum FN, Lewis EC, Voelkel N, Dinarello CA, **Abbate A**. Alpha-1 antitrypsin inhibits caspase-1 and protects from acute myocardial ischemia-reperfusion injury. ***J Mol Cell Cardiol*** 2011;51:244-51. doi: 10.1016/j.yjmcc.2011.05.003. PubMed PMID: 21600901.

b) **Abbate A**, Van Tassell BW, Christopher S, Abouzaki NA, Sonnino C, Oddi C, Carbone S, Melchior RD, Gambill ML, Roberts CS, Kontos MC, Peberdy MA, Toldo S, Vetrovec GW, Biondi-Zoccai G, Dinarello CA. Effects of Prolastin C (Plasma-Derived Alpha-1 Antitrypsin) on the acute inflammatory response in patients with ST-segment elevation myocardial infarction (from the VCU-alpha 1-RT pilot study). ***Am J Cardiol*** 2015 Jan 1;115(1):8-12. doi: 10.1016/j.amjcard.2014.09.043. PubMed PMID: 25456867.

c) Toldo S, Austin D, Mauro AG, Mezzaroma E, Van Tassell BW, Marchetti C, Carbone S, Mogelsvang S, Gelber C, **Abbate A**. Low-Density Lipoprotein Receptor-Related Protein-1 Is a Therapeutic Target in Acute Myocardial Infarction. ***JACC Basic Transl Sci***. 2017 Oct 30;2(5):561-574. doi: 10.1016/j.jacbts.2017.05.007. eCollection 2017 Oct. Erratum in: JACC Basic Transl Sci. 2018 Mar 01;3(1):162. PubMed PMID: 30062170; PubMed Central PMCID: PMC6058925.

d) Potere N, Del Buono MG, Mauro AG, **Abbate A**, Toldo S. Low Density Lipoprotein Receptor-Related Protein-1 in Cardiac Inflammation and Infarct Healing. ***Front Cardiovasc Med*** 2019 Apr 26;6:51. doi: 10.3389/fcvm.2019.00051. Review. PubMed PMID: 31080804; PubMed Central PMCID: PMC6497734.

**4. Exercise intolerance in heart failure**

Exercise intolerance is a cardinal symptom in heart failure associated with poor function, impaired quality of life, and unfavorable prognosis. The mechanism by which heart diseases induce impaired cardiac reserve, and how cardiac reserve and other extra-cardiac factors impact exercise capacity in patients with heart failure is still incompletely understood. Our team has used cardiopulmonary exercise testing with expiratory gas analysis and cardiac imaging to address these questions and investigate the role of systemic inflammation. This research has been supported by National Heart Lung and Blood Instititute R34 and R61/R33 grants, and a R01 award from the National Institute of Aging.

*Selected publications related to this topic:*

a) Van Tassell BW, Arena RA, Toldo S, Mezzaroma E, Azam T, Seropian IM, Shah K, Canada J, Voelkel NF, Dinarello CA, **Abbate A**. Enhanced interleukin-1 activity contributes to exercise intolerance in patients with

systolic heart failure. ***PLoS One***. 2012;7(3):e33438. doi: 10.1371/journal.pone.0033438. Epub 2012 Mar 16. PMID: 22438931; PMCID: PMC3306393.

b) Del Buono MG, Arena R, Borlaug BA, Carbone S, Canada JM, Kirkman DL, Garten R, Rodriguez-Miguelez P, Guazzi M, Lavie CJ, **Abbate A**. Exercise Intolerance in Patients With Heart Failure: JACC State-of-the-Art Review. ***J Am Coll Cardiol***. 2019 May 7;73(17):2209-2225. doi: 10.1016/j.jacc.2019.01.072. PMID: 31047010.

c) van Wezenbeek J, Canada JM, Ravindra K, Carbone S, Kadariya D, Trankle CR, Wohlford G, Buckley L, Del Buono MG, Billingsley H, Viscusi M, Tchoukina I, Shah KB, Arena R, Van Tassell B, **Abbate A**. Determinants of Cardiorespiratory Fitness in Patients with Heart Failure Across a Wide Range of Ejection Fractions. ***Am J Cardiol***. 2020 Jan 1;125(1):76-81. doi: 10.1016/j.amjcard.2019.09.036. Epub 2019 Oct 10. PMID: 31703805.

d) Del Buono MG, Mihalick V, Damonte JI, Billingsley H, Vecchiè A, Trankle CR, Kadayira D, Wohlford G, Ho AC, Talasaz A, Carbone S, Markley R, Turlington J, Lu J, Federmann E, Arena R, Van Tassell B, **Abbate A**, Canada JM. Preservation of Cardiac Reserve and Cardiorespiratory Fitness in Patients With Acute De Novo Versus Acute on Chronic Heart Failure With Reduced Ejection Fraction. ***Am J Cardiol***. 2021 Nov 1;158:74-80. doi: 10.1016/j.amjcard.2021.07.036. Epub 2021 Aug 29. PMID: 34465455; PMCID: PMC8497420.

**5. Pericarditis, COVID-19 and other cardio-immunology topics**

The interest in IL-1 and the inflammasome has led our team to investigate other immunology topics in which IL-1 blockers could be developed into therapeutics. **Acute and recurrent pericarditis**, a condition that remained poorly understood, known to be characterized by enhanced inflammation and to anecdotally respond to IL-1 blockers. We created a translational program in pericarditis that included human pathology samples, pre-clinical model of disease and clinical trials. In 2020 given our background in IL-1 biology, we became involved early in the studies aimed at understanding the pathophysiology of COVID-19 pneumonia and clinical research with cytokine inhibitors. This research has been supported by internal funds, by investigator-initiated industry sponsored grants, and by participation in multi-center clinical trials.

*Selected publications related to this topic:*

a) Chiabrando JG, Bonaventura A, Vecchié A, Wohlford GF, Mauro AG, Jordan JH, Grizzard JD, Montecucco F, Berrocal DH, Brucato A, Imazio M, **Abbate A**. Management of Acute and Recurrent Pericarditis: JACC State-of-the-Art Review. ***J Am Coll Cardiol***. 2020 Jan 7;75(1):76-92. doi: 10.1016/j.jacc.2019.11.021. PMID: 31918837.

b) Mauro AG, Bonaventura A, Vecchiè A, Mezzaroma E, Carbone S, Narayan P, Potere N, Cannatà, Paolini JF, Bussani R, Montecucco F, Sinagra G, Van Tassell BW, **Abbate A**, Toldo S. The role of NLRP3 inflammasome in pericarditis: potential for therapeutic approaches. ***JACC Basic Transl Sci*** 2021;6:137-150.

c) Klein AL, Imazio M, Cremer P, Brucato A, **Abbate A**, Fang F, Insalaco A, LeWinter M, Lewis BS, Lin D, Luis SA, Nicholls SJ, Pano A, Wheeler A, Paolini JF; RHAPSODY Investigators. Phase 3 Trial of Interleukin-1 Trap Rilonacept in Recurrent Pericarditis. ***N Engl J Med***. 2020 Nov 16. doi: 10.1056/NEJMoa2027892. Epub ahead of print. PMID: 33200890.

d) Caricchio R, **Abbate A**, Gordeev I, Meng K, Hsue PY, Neogi T, Arduino R, Fomina D, Bogdanov R, Stepanenko T, Ruiz Seco P, Gonzalez Garcia A, Chen Y, Li Y, Whelan S, Noviello S, for the CAN-COVID Investigators. Effect of canakinumab vs placebo on survival without invasive mechanical ventilation in patients hospitalized with severe COVID-19: a randomized clinical trial. ***JAMA*** 2021 Jul 20;326(3):230-239. doi: 10.1001/jama.2021.9508. PMID: 34283183; PMCID: PMC8293025.

For a full list of publications https://www.ncbi.nlm.nih.gov/myncbi/antonio.abbate.1/bibliography/public/

*Peer reviewed publications*: >**550** *Google Scholar citations*: **37,388** *Google Scholar H-index:* **105**