

## BIOGRAPHICAL SKETCH

NAME: **Moneghetti, Kegan James**

POSITION TITLE: Clinical Assistant Professor, Cardiovascular Division, School of Medicine, Stanford University

### EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	Completion Date MM/YYYY	FIELD OF STUDY
Monash University, Melbourne, Australia	MBBS (hons)	11/2006	Medicine
Royal Australian College of Physicians, Australia	FRACP	12/2013	Cardiovascular Medicine
Stanford University, California, USA	Post-doc	11/2018	Exercise Physiology
University of Melbourne, Melbourne, Australia	PhD	03/2019	Cardiovascular Medicine

### A. Personal Statement

I have the expertise, training and leadership required to successfully implement the proposed research project. As a cardiologist with expertise in exercise physiology I have observed the heterogeneity in which human subjects with and without disease respond to a bout of exercise. Through collaborative research I have developed with knowledge and skills in the expanding discipline of immune profiling, omics and precision medicine. Our collaborative research strategy has harnessed these responses to help differentiate disease.

I bring a unique skill set to this proposal as a clinical cardiologist have been had extensive experience is cardiac diagnostics and training in cardiopulmonary exercise testing during my post-doctoral fellowship at Stanford University. Using these skills, I have shown the usefulness of exercise testing in discriminating and prognosticating subgroups of cardiomyopathy. [1,2] Through collaboration with experts in the fields of diabetes and genomics I have worked to help better identify disease and investigate the mechanisms of the disease modifying effects of exercise. [3] Collaborating with the ME/CFS initiative we demonstrated the usefulness of exercise to help define better discriminate this condition. We found differences in absolute heart rate recovery slope and cytokine profiling between cases and control post exercise. [4]

- **Moneghetti KJ**, Giraldeau G, Wheeler MT, Kobayashi Y et al. Incremental value of right heart metrics and exercise performance to well-validated risk scores in dilated cardiomyopathy. *Eur Heart J Cardiovasc Imaging*. 2018 Aug 1;19(8):916-925
- **Moneghetti KJ**, Stolfo D, Christle JW, Kobayashi Y, Value of Strain Imaging and Maximal Oxygen Consumption in Patients With Hypertrophic Cardiomyopathy. *Am J Cardiol*. 2017 Oct 1;120(7):1203-1208.
- Schüssler-Fiorenza Rose SM, Contrepolis K, **Moneghetti KJ**, Zhou W, et al. A longitudinal big data approach for precision health. *Nat Med*. 2019 May;25(5):792-804.

- **Moneghetti KJ**, Skhiri M, Contrepolis K, Kobayashi Y et al. Value of Circulating Cytokine Profiling During Submaximal Exercise Testing in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Sci Rep*. 2018 Feb 9;8(1):2779.

## B. Positions and Honors

### Positions and Employment

12/2018 -	Instructor, Cardiovascular Division, School of Medicine, Stanford University, CA
08/2015 - 11/2018	Post-doctoral Fellow, Cardiovascular Institute, Stanford University, CA
02/2015 – 07/2018	Staff Cardiologist, Monash Heart, Melbourne, Australia
02/2014 – 01/2015	Cardiovascular Imaging Fellow, Monash Heart, Melbourne, Australia
02/2013 – 01/2014	Senior Cardiology Fellow, Alfred Hospital, Melbourne, Australia
02/2011 – 01/2012	Cardiology Fellow, St Vincent's Hospital, Melbourne, Australia
02/2008 – 01/2011	Medical Resident/Fellow, Alfred Hospital, Melbourne, Australia
01/2007 – 01/2008	Medical Intern, Alfred Hospital, Melbourne Australia

### Honors

2016	Stanford Cardiovascular Travel Award
2009	Young Investigator Award, 3rd Joint Congress of the APSR/ACCP

## C. Contribution to Science

1. *Optimization of data acquired during cardiovascular diagnostics*. My early work address in increasing amount parameters being assessed during echocardiography and these data's association with exercise capacity. The lack of integration of quantitation exercise performance which is strongly associated with mortality, was an opportunity to optimize the use of both echocardiography and exercise testing. In collaboration with the Clinical Biomarker and Phenotype Core Laboratory (BPCL) and Stanford Cardiopulmonary Exercise Testing Laboratory we created the Stanford Exercise Testing Registry to address this unmet need. Our findings have suggested that the integration of both novel echocardiographic parameters and maximal oxygen consumption (exercise performance) and improved risk stratification in heart failure beyond gold standard risk score in the field. This work has formed the basis for the methodology of larger precision health studies within the school of medicine at Stanford University.

- **Moneghetti KJ**, Kobayashi Y, Christle JW, Ariyama M et al. Contractile reserve and cardiopulmonary exercise parameters in patients with dilated cardiomyopathy, the two dimensions of exercise testing. *Echocardiography*. 2017 Aug;34(8):1179-1186.
- Kobayashi Y, **Moneghetti KJ**, Boralkar K, Amsallem M et al. Challenging the complementarity of different metrics of left atrial function: insight from a cardiomyopathy-based study *Eur Heart J Cardiovasc Imaging*. 2017 Oct 1;18(10):1153-1162.
- **Moneghetti KJ**, Giraldeau G, Wheeler MT, Kobayashi Y et al. Incremental value of right heart metrics and exercise performance to well-validated risk scores in dilated cardiomyopathy. *Eur Heart J Cardiovasc Imaging*. 2018 Aug 1;19(8):916-925
- **Moneghetti KJ**, Stolfo D, Christle JW, Kobayashi Y, Value of Strain Imaging and Maximal Oxygen Consumption in Patients with Hypertrophic Cardiomyopathy. *Am J Cardiol*. 2017 Oct 1;120(7):1203-1208.

2. *Defining the interaction between inflammation and echocardiographic phenotypes*. The relationship between cardiovascular disease and inflammation has been well described,

however, there is limited understanding in how these markers related to novel echocardiographic metrics. Working with the Human Immune Monitoring Center (HIMC) and interventional cardiology group we assess the role of serum biomarkers that represent inflammation and ventricular remodeling parameters assessed with echocardiography. We demonstrated that growth differentiation factor 15 was associated with lack of ventricular recovery and the specific cytokines profiles favor adverse remodeling in those patients undergoing transcatheter aortic valve replacement. This has implications for the field by highlighting possible therapeutic targets and adding tools that could identify those patients at high risk post valve replacement.

- Kim JB, Kobayashi Y, **Moneghetti KJ**, Brenner DA et al. GDF-15 (Growth Differentiation Factor 15) Is Associated With Lack of Ventricular Recovery and Mortality After Transcatheter Aortic Valve Replacement. *Circ Cardiovasc Interv.* 2017 Dec;10(12).
- Kim JB, Kobayashi Y, Kuznetsova T, **Moneghetti KJ** et al. Cytokines profile of reverse cardiac remodeling following transcatheter aortic valve replacement. *Int J Cardiol.* 2018 Nov 1;270:83-88.

3. *Advanced the field of pre-participation screening in athletes through echocardiography.* Pre-participation screening is performed at a growing number of colleges and universities. While the majority evaluations rely upon physical examinations and often include electrocardiograms, echocardiography is being integrated in many screening programs. The heterogeneity of physiological adaptation has made thresholds for risk hard to define. We have investigated the ability of preparticipation to identify those at risk and proposed specific metrics, that may be useful in identifying those athletes who required more in depth phenotyping before being cleared to play.

- **Moneghetti KJ**, Singh T, Christle JW, Kooreman Z, Kobayashi Y, Bouajila S, Wheeler M, La Gerche A, Ashley E, Froelicher V, Haddad F. Ventricular Remodeling in Division I College Football Players, the Importance of Race, Position and Body Composition [In press].
- Hedman K, **Moneghetti KJ**, Christle JW, et al Blood pressure in athletic preparticipation evaluation and the implication for cardiac remodeling *Heart* Published Online First: 28 May 2019
- Kooreman Z, Giraldeau G, Finocchiaro G, **Moneghetti K** et al. Athletic Remodeling in Female College Athletes: The "Morganroth Hypothesis" Revisited. *Clin J Sport Med.* 2019 May;29(3):224-231.

4. *Extending the indication of exercise testing and echocardiography outside cardiovascular disease.* Through the investigation of echocardiography and biomarkers it became apparent that the ability of cytokines and exercise to differentiate cardiovascular disease may be relevant to fields outside of cardiovascular medicine. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome affects almost 3 million people, which consist of a profound adverse reaction to exercise known as post exertional malaise. One hypothesis of ME/CFS is immune dysregulation, therefore, by combining immune profiling with exercise we found contrasting cytokines networks between cases and controls and identified a group of cytokines including CD40 ligand which differentiated those with disease. Working with the Integrated Personalized Omics Profiling Initiative we extended this work by performing multi-omic profiling from a well-characterized group of participants with regards to glucose regulation (e.g. insulin resistance and diabetes status), presenting the concept of the personalized exercise test for the first time. This work will be used to understand the mechanisms behind the benefits of exercise and to explain individual exercise performance.

- **Moneghetti KJ**, Skhiri M, Contrepolis K, Kobayashi Y et al. Value of Circulating Cytokine Profiling During Submaximal Exercise Testing in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Sci Rep.* 2018 Feb 9;8(1):2779.
- Schüssler-Fiorenza Rose SM, Contrepolis K, **Moneghetti KJ**, Zhou W, et al. A longitudinal big data approach for precision health. *Nat Med.* 2019 May;25(5):792-804.

A complete list of my work:

[www.ncbi.nlm.nih.gov/myncbi/kegan%20james.moneghetti.1/bibliography/public/](http://www.ncbi.nlm.nih.gov/myncbi/kegan%20james.moneghetti.1/bibliography/public/)

## D. Research Support

### Ongoing Research Support

NIH, 12/01/2018 -

#### *Exercise and Immune Profiling in ME/CFS*

The objective of this project is to utilize methods and insights recently established by the Milieu Intérieur Consortium to obtain a more accurate representation of immunological function in ME/CFS at and in the context of a bout of acute exercise.

Verily, 07/01/2017 -

#### *Project Baseline*

Project Baseline is an initiative to make it easy and engaging for people like you to contribute to the map of human health and participate in clinical research. Together with researchers, clinicians, engineers, designers, advocates, and volunteers, we're collaborating to build the next generation of healthcare tools and services.

Intermountain-Stanford Collaboration Grant, 07/01/2017 -

#### *Application of risk scores to heart failure with preserved ejection fraction*

The aim of this study is to validate the Intermountain Risk Score (IMRS) and Get with Guidelines heart failure risk score in inpatient population with heart failure preserved ejection fraction.