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EDITORIAL

Best Paper of the Year 2022

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Twelve months ago, we introduced a new section in JCTR that highlights the best papers of the previous year [1]. In 2022, there were again numerous relevant and robust manuscripts published in JCTR. Among these, the associate editors felt the following papers stood out based on their novelty, scientific rigor, and translational impact. We believe that they showcase the quality and diversity of the papers published in JCTR.

Best Paper of the Year

Harnessing the Plasma Proteome to Mirror Current and Predict Future Cardiac Remodeling After Myocardial Infarction, by Upendra Chalise and Colleagues [2].

The authors of this year's best JCTR paper sought to identify predictors of adverse remodeling and progression to heart failure post-myocardial infarction (MI). Using three different experimental setups, with murine and human data, they retrospectively identified and prospectively validated plasma markers that reflected and predicted adverse cardiac remodeling after MI.

MI is a precursor for adverse cardiac remodeling and heart failure. The initial ischemic event is followed by metabolic and ionic changes that trigger a cascade of changes that can irreversibly alter the anatomy and physiology of the heart. The changes include necrosis, apoptosis, inflammation, fibrosis, extracellular matrix modification, chamber wall thinning, conduction disorders, loss of cardiac function, LV dilation, neurohormonal changes, and arrythmias. While there is commonality in the responses, the timing and extent of each change are highly variable. This heterogeneity of response makes the development and assessment on new therapies aimed at modifying these changes extremely difficult, especially as one translates findings from a highly controlled lab environment, with homogenous ischemic events, CV disease histories, and genetic profiles, to a heterogeneous clinical setting.

By correlating echocardiography and proteome array data from murine cohorts, Chalise and colleagues identified 5 possible markers of adverse cardiac remodeling at day 3 post-MI. They then prospectively tested these markers in a second murine study and found that 4 of the markers (ApoA1, IgA, IL-17E, and TIMP-1) again correlated with echocardiographic changes in LV volume and function at day 7 post-MI. The authors further investigated protein–protein interactions for each of the markers in a human glycoprotein array and found that cytokine–cytokine receptor signaling was the top enriched KEGG pathway for the candidates.

A unique aspect of the findings was the stability of these markers across time, given how quickly the post-MI milieu changes, making many other markers less reliable. This is translationally relevant because, in addition to characterizing key post-infarction pathophysiological mechanisms, it may help address an unmet clinical need, which is the ability to predict the trajectory of infarcted patients. The identification of at-risk patients has the potential to enable smaller, faster, and less expensive clinical trials, potentially leading to personalized therapies and lower costs to the healthcare system.

Highly Commended Papers in JCTR in 2022

Dickkopf1 (Dkk1) Alleviates Vascular Calcification by Regulating the Degradation of Phospholipase D1 (PLD1), by Xuan Li and Colleagues [3].

In this paper, the authors show that Dkk1 can prevent vascular calcification by promoting PLD1 protein degradation through the autophagolysosomal pathway. This paper is of clinical significance for the treatment of various diseases

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caused by vascular calcification, including atherosclerosis, systolic hypertension, and coronary heart disease. The combination of Dkk1 and autophagy provides a potential target and treatment for clinical vascular calcification related diseases.

Dual Specific Phosphatase 7 Exacerbates Dilated Cardiomyopathy, Heart Failure and Cardiac Death by Inactivating the ERK1/2 Signaling Pathway, by Jing Liu and Colleagues [4].

The physiological and pathological relevance of DUSPs in cardiovascular diseases remain largely unknown. Combining in vivo and in vitro approaches, Liu et al. found that DUSP7 overexpression exacerbated dilated cardiomyopathy, heart failure, and cardiac death by inactivating MAPK/ERK1/2 signaling. The study identified new therapeutic targets and new clinical pathways for alleviating dilated cardiomyopathy as well as improving cardiac function.

Transjugular Transcatheter Tricuspid Valve Implantation of LuX-Valve Bioprosthesis in a Preclinical Model, by Xiao-Ping Ning and Colleagues [5].

In this translational study, the authors used a sheep model to test the feasibility and safety of the LuX-Valve transjugular tricuspid valve (TV) replacement apparatus and to optimize the implantation procedure before a first-in-man study. The procedure was successful in six out of eight animals and provides a promising alternative for TR patients who are at high risk for open-heart surgery.

Association Between Circulating CD4⁺ T Cell Methylation Signatures of Network-Oriented SOCS3 Gene and Hemodynamics in Patients Suffering Pulmonary arterial Hypertension, by Giuditta Benincasa and Colleagues [6].

In this exciting paper, the authors used reduced representation bisulfite sequencing to identify differentially methylated CpG sites in circulating $CD4^+$ T cells isolated from patients with pulmonary artery hypertension (PAH). This was the first network-oriented study integrating circulating $CD4^+$ T-cell DNA methylation signatures, hemodynamic parameters, and validation experiments in PAH patients at first diagnosis or early follow-up. Promoter-restricted network and functional analyses revealed the association of SOCS3 gene methylation with PAH, unveiling its potential as therapeutic target and/or prognostic biomarker.

NO-Donation Increases Visceral Circulation in a Porcine Model of Abdominal Hypertension, by Per Skoog and Colleagues [7].

In this paper, the authors tested the effect of a nitric oxide (NO) donor on visceral circulation in a pig model of intraabdominal hypertension (IAH), which can lead to multiorgan failure. They demonstrated that the NO donor improved intestinal microcirculation, decreased arterial pressure, increased cardiac index, and reduced systemic and pulmonary vascular resistances. These results open new possibilities to improve intestinal microcirculation in IAH patients and increase survival in the ICU, although further research is needed before translating these findings to humans.

References

1. Xiao J, Lara-Pezzi E. Best paper of the year 2021. J Cardiovasc Transl Res. 2022;15(1):1–2.
2. Chalise U, Becirovic-Agic M, Rodriguez-Paar JR, Konfrst SR, de Morais SDB, Johnson CS, et al. Harnessing the plasma proteome to mirror current and predict future cardiac remodeling after myocardial infarction. J Cardiovasc Transl Res. 2022. https://doi.org/10.1007/s12265-022-10326-w.
3. Li X, Liu X-L, Li X, Zhao Y-C, Wang Q-Q, Zhong H-Y, et al. Dickkopf1 (Dkk1) Alleviates vascular calcification by regulating the degradation of phospholipase D1 (PLD1). J Cardiovasc Transl Res. 2022;15(6):1327–39.
4. Liu J, Yin Y, Ni J, Zhang P, Li W-M, Liu Z. Dual specific phosphatase 7 exacerbates dilated cardiomyopathy, heart failure, and cardiac death by inactivating the ERK1/2 signaling pathway. J Cardiovasc Transl Res. 2022;15(6):1219–38.
5. Ning X-P, Cao J-Y, Li M-X, Wang H, Li N, Song Z-G, et al. Transjugular transcatheter tricuspid valve implantation of LuX-valve bioprosthesis in a preclinical model. J Cardiovasc Transl Res. 2022. https://doi.org/10.1007/s12265-022-10325-x.
6. Benincasa G, Maron BA, Affinito O, D'Alto M, Franzese M, Argiento P, et al. Association between circulating CD4+ T cell methylation signatures of network-oriented SOCS3 gene and hemodynamics in patients suffering pulmonary arterial hypertension. J Cardiovasc Transl Res. 2022. https://doi.org/10.1007/s12265-022-10294-1.
7. Skoog P, Seilitz J, Oikonomakis I, Hörer TM, Nilsson KF. NO-donation increases visceral circulation in a porcine model of abdominal hypertension. J Cardiovasc Transl Res. 2022. https://doi.org/10.1007/s12265-022-10299-w.