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JAK-STAT
Getting to the heart of the matter

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In this issue of *JAK-STAT*, we introduce a series of reviews overlooking the ever-expanding field of myocardial JAK-STAT signaling. The history of cardiac JAK-STAT research begins in the mid-nineties, when various groups began to focus their attention on how myocardial physiology was specifically regulated through JAK-STAT signaling. Interest in the area began to grow following initial observations by the groups of Kishimoto and Chien, who were among the first to show that cardiac myocytes possess a functional gp130/JAK-STAT system that was intimately involved in the regulation of cardiac hypertrophy.[1-3] Not long after, it was appreciated that STAT cardiac activity could be regulated by a host of diverse factors, including cardiotrophin-1, angiotensin II, leukemia inhibitory factor (LIF) and insulin, all of which suggested a that diverse and interesting underlying biology was at play.[4-7] Several groups went on to characterize the activities and downstream effects of STAT1 and STAT3 in a host of cardiovascular pathologies.[8] In an exciting series of discoveries for the field, the JAK-STAT pathway was found to play a fundamental role in the protective effects of both pre- and post- conditioning.[9,10] The advent of cardiac-specific STAT-deficient mice further reinforced the essential requirement of STATs for normal myocardial functioning, an area in which the contributions of the late Helmut Drexler will be sorely missed.[11,12] Recent discoveries such as the role of STATs in the development of cardiac stem cells and in controlling mitochondrial respiration have led to renewed enthusiasm in the field and set the stage for exciting times ahead in this area of cardiac research.[13,14]

In this issue of *JAK-STAT*, some of the foremost experts in the field have come together to present the state of play in cardiovascular JAK-STAT biology. Frias et al. discuss recent exciting data showing that the sphingosine-1 phosphate (S1P) component of high density lipoproteins (HDL) exerts strong cardioprotective activity through the recently characterized survivor activating factor enhancement (SAFE) pathway.[15] Booz and colleagues tackle the difficult question of trying to understand the many modes of STAT3 activity in the heart and examine the issue of differential signaling downstream of IL-6 family cytokines.[16] Knight et al. review the recent findings that have uncovered how STAT1 and STAT3 regulate myocardial cell death during I/R injury, post-infarct remodeling and ischemic conditioning.[17] Kishore and Verma discuss the cardioprotective actions of STAT3 and in particular the recent finding that IL-10, acting though STAT3, promotes increases survival of endothelial progenitor cells and vascularization of the heart.[18] Fujio and colleagues discuss the timely topic of JAK-STAT signaling in cardiac stem cells with a focus on their recent work characterizing JAK-STAT mediated endothelial differentiation of Sca1$^+$ cardiac progenitor cells through the kinase Pim-1.[19] Finally, Wagner and Siddiqui focus on IL-6 trans-signaling, the intersection of the JAK-STAT and GPCR pathways and how components of the JAK-STAT pathway interact with the basal transcription machinery.[20]

The story of myocardial JAK-STAT biology has led to intriguing and unexpected findings over the years and researchers continue to uncover novel ways in which the JAK-STAT pathway controls cardiac health, homeostasis and pathology. We must also be mindful that along with significant advances in

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Dr Barry received his PhD from University College London under the supervision of Prof. David Latchman and Dr Anastasis Stephanou. There he studied the role of STAT transcription factors in regulating cell fate following ischemic injury, oxidative stress and DNA damage. During his PhD, Dr Barry also spent time in the group of Prof. Richard Flavell at Yale where he developed an interest in immune regulation. This has led to his recent interest in understanding how pro-inflammatory cytokines contribute to myocardial ischemic injury. In particular he has focused on how IL-17 production during myocardial infarction leads to local chemokine release and subsequent neutrophil mediated tissue damage in the heart. Currently Dr Barry is an IRCSET research fellow at Trinity College Dublin where he is continuing his work on myocardial inflammation with Prof. Padraic Fallon.

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basic research, there is still a great unmet need for new therapies in cardiovascular disease. As we look to the future, the onus is on us all to expand upon the significant understanding we have gained in how the JAK-STAT pathway influences cardiac biology and use it as a platform to improve human cardiovascular health.

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