bone formation and broader differentiation into mesoderm-like cells in vitro. While some of their biological characteristics are documented in vitro, their role in the aging process and the pathogenesis of musculoskeletal diseases remains yet to be thoroughly evaluated. This translational session will go from bench to bedside, reviewing the current evidence on COP cells. In this session, we will provide an overview of the role of COP cells in the aging process and a number of physiological and pathological conditions and identify areas for future research. In addition, we will suggest possible areas for clinical utilization in the management of musculoskeletal diseases, which include novel diagnostic and therapeutic uses.

COP CELLS AND TISSUE LOSS SYNDROMES: FRAILTY, SARCOPENIA, AND OSTEOPOROSIS
Gustavo Duque, The University of Melbourne, St Albans, Victoria, Australia

COP cells have been identified as having a potential role in the pathogenesis of tissue loss syndromes such as osteoporosis and frailty. This is based on the hypothesis that their dysregulation may cause a decrease in bone and muscle formation, which also increase the risk of adverse outcomes such as frailty and disability. Whereas high numbers of COP cells have been associated with osteoporosis and fracture healing, a low percentage of COP (%COP) cells have been associated with frailty and disability. In addition, low expression of lamin A (a protein of the inner nuclear envelope) in COP cells has also been associated with frailty and disability in older persons. In this session, the evidence on quantification methods for COP cells in clinical settings and the potential clinical use of COP cells in tissue loss syndromes will be discussed. This discussion will include current evidence supporting the use of COP cells as a biomarker or as a novel therapeutic approach to these age-related conditions.

COP CELLS IN STATES OF BONE ANABOLISM AND ABNORMAL CALCIFICATION/OSSIFICATION
Robert Pignolo, Mayo Clinic College of Medicine, Rochester, Minnesota, United States

Circulating osteogenic progenitor (COP) cells are a population of cells in the peripheral blood with the capacity for bone formation, as well as broader differentiation into mesoderm-like cells in vitro. There are several pathologies of accelerated bone formation and physiological responses to injury in which COP cells have been theorized to play a role. These include fracture, vascular calcification, and subtypes of heterotopic ossification (HO). Overall, the available studies suggest COP cells are likely to be mobilized in response to fracture, home to the site of injury, undergo a maturation process, and contribute to the osteogenesis and angiogenesis required for fracture healing. HO is the pathological process of bone formation in nonskeletal tissue and can be acquired or hereditary. COP cells may seed sites of injury and inflammation that precede the formation of endochondral bone identified in both genetic and nongenetic forms of HO. Vascular calcification is a common occurrence in older adults and is strongly associated with poorer cardiovascular health outcomes. It appears that COP cells, particularly those expressing hematopoietic and vascular markers such as CD45 and CD34, contribute to the calcification and ossification of atherosclerotic plaques and aortic valves, and that they correlate to the severity of the calcification. Whether COP cells are attracted to sites of injury and inflammation and so are highly associated with fracture, vascular calcification/ossification and HO, or whether they underlie these processes at a more mechanistic level, remains to be more clearly demonstrated.

THE BIOLOGY OF COP CELLS: MESENCHYMAL OF HEMATOPOIETIC?
Meghan McGee-Lawrence, Medical College of Georgia, Augusta University, Augusta, Georgia, United States

Circulating osteogenic precursor (COP) cells constitute a recently discovered population of circulating progenitor cells with the capacity to form not only bone but other mesenchymal tissues. A small but growing body of literature explores these cells, but with a great deal of disagreement and contradiction within it, mainly whether these cells are from mesenchymal or hematopoietic origin. This session will discuss the origins and biological characterization of these cells, including the identification strategies used to isolate these cells from the peripheral blood. It also examines the available knowledge on the in vitro and in vivo behaviour of these cells in plastic adherence, differentiation capacity, proliferation, and cellular homing. We will also review the profound and exciting implications for future use of COP cells in clinical practice, particularly in comparison with other types of stem cells.

THE KYNYRENINE PATHWAY METABOLITES QA AND KYNA INDUCE SENESCENCE IN BONE MARROW STEM CELLS THROUGH THE AHR PATHWAY
Dmitry Kondrikov,1 Ahmed Elmansiri,2 Xing-ming Shi,3 Meghan McGee-Lawrence,4 Sadanand Fulzele,5 Mark Hamrick,6 Carlos Isales,7 and William Hill,2 1. Medical University of South Carolina, Medical University of South Carolina, South Carolina, United States, 2. Medical University of South Carolina, Charleston, South Carolina, United States, 3. Augusta University, Augusta, Georgia, United States, 4. Medical College of Georgia, Augusta University, Augusta, Georgia, United States, 5. Medical College of Georgia, Augusta, Georgia, United States

Cell senescence is emerging as a critical factor in the pathophysiology of aging bone loss. We have shown that the essential amino acid tryptophan is metabolized by IDO-1 in the periphery to generate kynurenine (KYN), and that KYN can signal through the aryl hydrocarbon receptor (AhR) transcription factor pathway to inhibit osteogenesis in bone marrow MSCs via epigenetic regulation of osteogenic genes, while also upregulating osteoclastogenic transcription factors and genes driving osteoclast activity. Further, we recently showed that KYN acting via AhR inhibits MSC autophagy while inducing senescence. Here we demonstrate that KYN metabolites downstream from KYN act via the AhR signaling pathway to inhibit autophagy and induce SASP expression and drive senescence in murine and human bone marrow MSCs. We focused on two of these metabolites, quinolinic acid (QA) and kynurenic acid (KYNA) and investigated their effects on BMSC cellular function.