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 KYNURENINE PATHWAY METABOLITES QA AND KYNA INDUCE SENESCENCE IN BONE MARROW STEM CELLS THROUGH THE AHR PATHWAY

Dmitry Kondrikov,[1] Ahmed Elmansi,[2] Xing-ming Shi,[3] Meghan McGee-Lawrence,[4] Sadanand Fulzele,[5] Mark Hamrick,[5] Carlos Isales,[5] and William Hill,[2]
1. Medical University of South Carolina, Meddical 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 though 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.

We demonstrated that both kynurenine pathway metabolites QA and KYNA increase biomarkers for senescence including beta-galactosidase, p21/Cdkn1 and other SASPs such as PAI-1 and TIMP-2, as well as nuclear DNA damage leading to senescent markers like H2A Ser139 phosphorylation, and the accumulation of senescence-associated hetero chromatin foci (SAHF) with H3K9-me3 labeling. Then upon treatment with the AhR inhibitor 3'4'-DMF the disruption of autophagy and induction of senescent biomarkers was blocked. Like KYN, the effects of QA and KYNA were mediated through the AhR receptor. Therefore, this presents novel therapeutic targets linked to KYN metabolite signaling via AhR to prevent senescence and bone loss.

Session 1175 (Symposium)

A TRANSITIONAL CARE MODEL FOR VETERANS WITH COMPLEX NEEDS DURING COVID: THE BEHAVIORAL RECOVERY OUTREACH (BRO) TEAM

Chair: Kathleen Matthews Discussant: Latrice Vinson

The Veterans Health Administration's Care for Patients with Complex Problems (CP)2 Program developed a national infrastructure to disseminate promising practice models to improve care for Veterans with complex medical, mental health, and/or neurocognitive conditions, who may also have behaviors disruptive to care. A strategic priority is improving safe and effective transitions to community care for Veterans with complex care needs, many of whom have historically been limited to VA settings as a result of behavioral concerns. The Behavioral Recovery Outreach (BRO) Team was the first model identified for national dissemination and evaluation at partner sites. Developed at VA Central Iowa, BRO is an interdisciplinary team model that identifies Veterans in long-term VA care settings with complex care needs to engage in individualized behavioral programing to manage/stabilize behaviors and safely transition them to more appropriate and less costly community settings. This symposium will describe the BRO team model, highlight the facilitators and barriers to nationally disseminating the BRO model with VA partner facilities, discuss adaptations in continuing community transitions following the COVID-19 pandemic, and describe program outcomes. The first speaker will discuss development of the BRO model and outcomes of a regional dissemination. The second speaker will present results from the program evaluation of the national dissemination. The final speaker will describe BRO Team expansion and lessons learned from the perspective of a VA partner facility. The (CP)2 Program Director will integrate findings and highlight implications for scaling and evaluating promising models for national dissemination for policy, practice, and future research.

EVALUATING IMPLEMENTATION OF THE BEHAVIORAL RECOVERY OUTREACH (BRO) TEAM: ONE YEAR OF IMPLEMENTATION

Jenefer Jedele,[1] Cameron Griffin,[2] Kathleen Matthews,[3] and Latrice Vinson,[4] *1. Veterans Health Administration, Ann Arbor, Michigan, United States, 2. VA, Ann Arbor, Michigan, United States, 3. VISN 23, Des Moines, Iowa, United States, 4. Department of Veterans Affairs, Department of Veterans Affairs, District of Columbia, United States*

We present evaluation results after one year of implementation by nine BRO Teams. Monthly checklists documented consistent composition across teams: a psychologist, social worker and nurse. Social workers were recognized as having a critical role in implementation, serving as a referral source and liaison between the CLC, Veteran/family, and community facility. Early implementation focused on team and program development with barriers including unprotected time for Team members. In the first year, the nine teams enrolled 70 Veterans, discharging 86% to community facilities. Characteristics of the Veterans suggest Teams are reaching the complex Veteran targeted by the model. Barriers to successful discharge include community facility inexperience/training and confidence to manage complex residents. COVID emerged as the leading barrier to outreach to internal and external partners and providing transitional support to the Veteran after discharge. We discuss the impact of these preliminary findings on future implementation and dissemination of the model.

THE BEHAVIORAL RECOVERY OUTREACH (BRO) TEAM: A TRANSITIONAL CARE MODEL FOR VETERANS WITH COMPLEX CARE NEEDS

Kathleen Matthews,[1] Grant Bauste,[2] and Emily Luitjens,[3] *1. VISN 23, Des Moines, Iowa, United States, 2. Minneapolis VA Medical Center, Minneapolis, Minnesota, United States, 3. St. Cloud VA Health Care System, St. Cloud, Minnesota, United States*

In 2012, VA Central Iowa developed a novel program known as the Behavioral Recovery Outreach (BRO) Team to address unmet needs of our aging Veteran population with complex medical, psychological, neurocognitive and behavioral concerns. BRO Teams provide evidence-informed treatments in inpatient VA settings, and transitional care/support post-discharge to ensure successful placement and stability in the community. We will discuss how implementation science informed the expansion of this model from a local pilot to a nationally disseminated program. We will explore the challenges of ensuring program fidelity while fostering innovation and adaptation. Given the challenges of national dissemination, we will highlight the predicted and unforeseen aspects of program evaluation and policy implications. Finally, we will discuss the impacts of the COVID-19 pandemic on delivery of care methods and community-based interactions, as well as how this program has improved the lives and quality of care for this high-risk Veteran population.

ROLLING OUT BEHAVIORAL RECOVERY OUTREACH (BRO) TEAMS: PERSPECTIVES FROM AN INAUGURAL PARTNER SITE

Trisha Gaudig, *Sioux Falls VA, Sioux Falls, South Dakota, United States*

The Sioux Falls VA Community Living Center (CLC) is a partner site for the Behavioral Recovery Outreach (BRO) Team dissemination. This CLC is home to over 55 Veterans requiring a variety of specialty needs such as dementia care,