of non-positive outcomes shows a bell-shaped curve: 1.4% of participants responded that cannabis use improved all outcomes, while 4.1% of participants answered that cannabis use did not. When looking at negative outcomes, 86% of participants reported none worsened, and 11% reported one of the outcomes was affected. Only a small fraction of the participants (3%) claimed more than one negative outcomes after cannabis use.

Session 4315 (Symposium)

THE HALLMARKS OF AGING: LEVERAGING ON THEIR INTERACTIONS

Chair: Ana Maria Cuervo
Co-Chair: Ronald Kohanski
Co-Chair: Viviana Perez

SELECTIVE AUTOPHAGY: A LINK ACROSS THE HALLMARKS OF AGING

Ana Maria Cuervo, *Albert Einstein College of Medicine, Bronx, New York, United States*

Autophagy function has been closely linked with the loss of proteostasis that characterizes most old organisms and tissues. However, the cellular functions of selective types of autophagy such as chaperone-mediated autophagy (CMA) go beyond cellular quality control. CMA can degrade fully functional proteins to terminate their function and thus contribute to regulation of multiple cellular processes. To fully understand the consequences of loss of CMA function with age, we have developed genetic and pharmacological ways to modulate this pathway in old mice. Our data supports involvement of CMA in other hallmarks of aging such as metabolism, senescence, cellular response to stress, epigenetics and cellular stemness. This interconnection among the cellular processes that drive aging highlights the potential of acting on only some of them with geroprotective effects.

ANTI-AGING INTERVENTIONS TARGETING THE HALLMARKS OF AGING

Brian Kennedy, *National University of Singapore, Singapore*

EFFECTS OF CALORIC RESTRICTION ON THE EPIGENETIC LANDSCAPE OF HEMATOPOIETIC STEM CELLS

Isabel Beerman, *NIA, Baltimore, Maryland, United States*

During aging, alterations of hematopoietic stem cells are associated with functional decline of the blood system. Caloric restriction (CR) interventions have been reported to improve adult stem cells in other tissue types during aging so we sought to evaluate the effects of CR on the aged HSC compartment. We find significant epigenetic alterations in HSCs isolated from aged mice after life-long CR compared to ad libitum fed aged mice. We further evaluated the epigenetic landscapes and functional potential of aged HSCs shortly after allowing life-long CR mice access to ad libitum food. We uncover epigenetic modification associated with functional alterations of the HSCs, defining potential mechanisms by which restrictions in food consumption affect the aging hematopoietic compartment.

CALORIC RESTRICTION MIMETICS ATTENUATE THE HALLMARKS OF AGING

Guido Kroemer, *University of Paris, Villejuif/Paris, Ile-de-France, France*

Nutrient depletion, which is one of the physiological triggers of autophagy, results in the depletion of intracellular acetyl coenzyme A (AcCoA) coupled to the deacetylation of cellular proteins. We found that there are at least 4 possibilities to mimic these effects, namely (i) the depletion of cytosolic AcCoA by interfering with its biosynthesis, (ii) the stimulation cytosolic AcCoA consumption, (iii) the inhibition of protein acetyltransferases, or (iii) the stimulation of protein deacetylases. Thus, AcCoA depleting agents, AcCoA-consuming agents, acetyltransferase inhibitors or deacetylase activators are highly efficient inducers of autophagy and reduce aging-associated diseases including diabetes, obesity, cardiac failure and failing cancer immunosurveillance. Hence, we classify them as "caloric restriction mimetics" (CRM). We have initiated the systematic search for CRMs based on their cellular effects in vitro. We built screening assays amenable to high-throughput technology for the identification of CRMs. These results will be discussed.

Session 4320 (Symposium)

WELL-BEING DURING THE COVID-19 PANDEMIC: THE ROLES OF AGE, RACE, AND GENDER

Chair: Nicky Newton
Discussant: Jennifer Lodi-Smith

In the early months of COVID-19, behavioral modifications (i.e., social distancing) were the only means available to ameliorate contagion. These had widespread ramifications for well-being, although older adults showed relatively less disruption and high resilience than their younger counterparts (Carney et al., 2021). Early findings highlight the need for a life course perspective when examining reactions to COVID-19, based on social structure, personal agency, and individual differences such as age, gender, and personality (Settersten et al., 2020). The presentations in this symposium contribute to a developing body of research that delves deeper into individual lived experiences during COVID-19. Using data from the Health and Retirement Study, Ryan examines cohort and age differences in pandemic-related social contact, communication, loneliness, and well-being for women in the US, revealing that the impact of pandemic-attributed psychosocial experiences on well-being differed by age group. Newton et al. examine associations between perceptions of future time, COVID-19 disruption, and psychological well-being among older Canadian women, finding that COVID-19 disruption moderated the relationship between constrained time horizons and well-being. Birditt and colleagues assessed racial disparities in relationships between COVID-related stress, social isolation, and depression among adults aged 18-97 from the Survey of Consumers, and found ethnic/racial minorities reported greater pandemic-related stress and that stress and social isolation had detrimental effects on well-being. A discussion by Lodi-Smith will emphasize the necessity to include individual differences – age, race, gender, cohort, cultural context –when examining pandemic-related well-being in order to provide a more nuanced body of research.