BUSTA A

LA CANDIDATA DESCRIVA "DAL MOMENTO CHE I MODULATORI EPIGENETICI CONTROLLANO I miRNA COME POSSONO ESSERE TECNICAMENTE VALUTATI QUESTI ULTIMI IN COLTURA"

Aging is a natural multifactorial process of structural and functional changes, affecting molecules, cells, and tissues, therefore, representing a main risk factor for several clinical phenotypes, including cardiovascular diseases and chronic conditions (1). It is undeniable that the incidence of cardiovascular diseases, mainly heart failure, increases in the elderly population (2). Global aging is a hallmark of our century: the eldery population comprise roughly 15% of the population, and this scenario will increase of an additional 25% on average by 2050 (www.globalaginginstitute.org). This unprecedented population profile will inevitably imply, among others, an increasing burden of cardiovascular events, some of which are directly linked to cellular senescence and dysfunction. Thus, increasing knowledge on the various mechanisms causing the progressive decline of cellular and tissue function may aid in developing therapies to delay or treat age-related conditions and diseases, such as diabetes, cardiovascular and neurodegenerative diseases (3). Consequently, the discovery of pathways responsible for increasing life span and health span, as both potential biomarkers and targets, is currently of primary interest.

BUSTA B

LA CANIDADATA DESCRIVA COME TECNICAMENTE POTREBBE ESSERE CONCEPITO IL SETTING SPERIMENTALE DI UN MODULATORE EPIGENETICO SU COLTURE CELLULARI

Since impairment in endogenous tissue function and repair is particularly exacerbated in the elderly persons and is involved in physiological aging and in chronic diseases (4), novel approaches of regenerative personalized medicine are being currently explored in order to ameliorate future therapeutic options for the aged society. Accordingly, several regenerative cell populations have been considered and tested in preclinical and clinical settings in the last years for cardiovascular applications, such as endothelial progenitor cells (EPCs) (5), mesenchymal stromal/stem cells (MSCs) (6), and resident cardiac progenitor cells (CPCs) (7, 8). Overall encouraging outcomes have been obtained in first clinical trials for several pathologies, such as revascularization strategies or cardiac cell therapy (5, 9), albeit with multiple issues still to be overcome (10).

BUSTA C

LA CANDIDATA DESCRIVA COME TESTARE TECNICAMENTE IN VIVO I MODULATORI EPIGENETICI

Endothelial progenitor cells are considered a main circulating stem cell population finely controlling vascular homeostasis and repair in physiological conditions (11–14), therefore representing an interesting crossroad between circulating markers, regenerative cells, and aging mechanisms. According to their intrinsic property, EPCs represent *per se* a valuable biomarker for monitoring pathological states, in particular those associated with vascular damage. Importantly, the demonstration that EPCs can be systemically recruited from the bone marrow-associated niche, and that after engraftment are able to replace old vasculature with new mature endothelial cells, has completely overturned the theory about aging (11, 12, 15) and can be considered a significant reference for the relationship between progenitor cells and aging. To date, EPCs represent one of the most studied example tools to rejuvenate the vascular system or to potentially delay the damages induced by aging. Specifically, aging implies, among others, profound derangements in the endothelium and consequently in EPCs in terms of either number or function, directly altering their ability to generate new vessels (16). Similarly, growth factors and hormones modulate endothelial function. According to this vision, endothelial responsiveness in both healthy subjects and patients with cardiac conditions has been improved by antiaging strategies based on administration of growth hormone (GH), which, among its many functions, has been reported to increase the number of circulating EPCs (17, 18). More importantly, in aged organisms where inflammation is exacerbated due to a dysregulated production of soluble mediators, a reduction in the biological properties of EPCs is consequently found. Mechanisms underlying these alterations are still to be fully elucidated, but are considered critical to unravel the modality by which a boosted turnover of the endothelial system can be achieved. However, they are hypothesized to be different when aging is the natural consequence of a physiological process compared to induced or premature aging, as after a pharmacological treatment.