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Rejuvenation Research

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Strategies for Engineered Negligible Senescence (SENS) Sixth Conference: Program and Abstracts

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CERNA BIOINFORMATIC ANALYSIS ON HUMAN TELOMERASE

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Messenger RNA (mRNA) translation efficiency is regulated by microRNAs. Each microRNA is able to regulate the translation of multiple mRNAs and each mRNA is regulated by multiple microRNAs. Thus, cellular mRNAs pool competes for microRNAs pool and viceversa. The regulatory network between mRNAs and microRNAs can be studied in the perspective of Competing Endogenous RNAs, or ceRNAs.

Here it is presented a bioinformatic study on ceRNAs for human telomerase (hTERT). Several genes potentially involved in the regulatory network of hTERT have been harvested by this study.

hTERT is essential for telomeres integrity. Telomere dysfunctions have been widely reported to be involved in Ageing, Cancer and Cellular Senescence.

Amongst the gene collected, the oncosupressor PTEN and the dynein heavy chain coding gene DNHD1 are top level interactors.

Interestingly, many genes of unknown functions result as predicted interactors, suggesting that hTERT may be involved in unexplored networks and scenarios.

Keywords: hTERT, telomerase, PTEN, dynein, CeRNA

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VASCULAR AGEING: CAUSES, MECHANISMS, COMPLICATIONS AND POSSIBLE THERAPEUTIC STRATEGIES

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Ageing is increasingly considered as an independent factor for the development of cardiovascular diseases (CDs). During ageing, there are structural and functional changes in the vasculature, including dilated lumen, altered intimal-medial thickness, vascular stiffness, endothelial dysfunction, increased endothelial apoptosis, matrix metalloproteinase dysregulation, increased expression of inflammatory molecules, aggravated oxidative stress and shortened telomere length. These changes leave the body and the arteries more susceptible to hypertension, atherosclerosis, medial degeneration and the onset of a different array of artery complications (i.e. myocardial infarction, stroke, aneurysms). Metabolic syndrome, obesity and diabetes are known to accelerate ageing process and, particularly, vascular ageing. In this presentation, most of these aspects will be described in the light of recent literature data and giving particular emphasis on those, which represent object of our studies. In particular, the data discussed in this report will be based on an expert opinion derived on the findings from author studies on ageing, age-related diseases and inflammation. On the other hand, our interest will be focused in proving potential working hypotheses about possible targets for the development of strategies both for prevention and improvement of the quality of life in elderly population.

Keywords: ageing, vascular ageing, cardiovascular diseases, new therapeutic strategies

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ACCELERATING TRANSLATIONAL RESEARCH PROCESSES FROM BENCH TO CLINIC

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The productivity of medical innovation has been in decline, and this threatens the commitment of both public and private funders. However, there are both disruptive technologies and disruptive ideas that promise a turnaround. CASMI (www.casmi.org.uk) is exploring both, and developing testable models for change - including new open innovation-based discovery models, adaptive licensing of medicines, the use of real world data in development, and the personalisation of therapy on both genomic and behavioural grounds. With the support of SENS, CASMI is also investigating the translational issues facing cell therapy, so that the highly promising science delivers patient benefit as speedily and affordably as possible.

Keywords: CASMI, Adaptive licensing, Open innovation, Real world data, Cell therapy

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TREATING AGE-RELATED MACULAR DEGENERATION THROUGH ENHANCED LYSOSOMAL DEGRADATION OF A2E

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Age Related Macular Degeneration (AMD) is the leading cause of visual loss among people 65 years and older. This disease manifests into two distinct forms, wet and dry. The pathogenesis for both forms is poorly understood and numerous hypothetical models have been studied to better understand their mechanism. The dry form of AMD involves atrophy of the retinal pigment epithelium (RPE) by the accumulation of bisretinoid lipofuscin within lysosomes as the cells phagocytose the outer membranes of the photoreceptors. A major fluorescent component of RPE lipofuscin is a compound known as pyridinum bisretinoid (A2E). We have been able to degrade A2E by exogenous enzyme delivery to cultured human RPE cells and cell free systems. We have discovered an enzyme (SENS20) that, in the presence of its co-substrate, has the ability to degrade A2E in a dose-dependent manner without damaging RPE cells. This dose-dependency is evident in vitro and in cell culture assays. Our studies show evidence for SENS20's positive enzymatic activity towards synthetic A2E cultured with human RPE cells and its ability for potential treatment of dry AMD.

Keywords: age-related macular degeneration, AMD, lipofusin, A2E, retinal pigmented epithelium

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SCREENING OF MEDICINAL PLANTS IN THE JUDEA REGION (ISRAEL) FOR GEROPROTECTIVE ACTIVITIES

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