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1. EFFECT OF PIRACETAM IN RESERPINE-INDUCED GASTRIC ULCERS IN RATS

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ABSTRACT

Nootropic drugs, which are widely used in the treatment of cognitive disorders and degenerative brain diseases, extend their therapeutic use to somatic and visceral pathology. We have investigated the effects of acutely administered piracetam on reserpine-induced gastric ulcers in rats. The drug effects are moderate and dose-dependent. In single doses, piracetam tends to aggravate ulcerogenesis. In case of repeated doses, a discrete protection is noticed.

Key words: gastric ulcers, piracetam, rats, reserpine.

2. THE ACTIVITY OF NADH AND NADPH MITOCHONDRIAL OXIDASE IN PSORIASIS

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ABSTRACT

This study aims to identify the markers in psoriasis, which might allow the quantifying of oxidative processes in the tissue. For this purpose, tissue biopsies were collected and the activity of two mitochondrial oxidant enzymes which intervene in the forming of superoxide anion was analyzed from a histoenzymologic point of view.

Key words: psoriasis, mitochondrial oxidases, superoxide anion.

3. THE EFFECTS OF DILTIAZEM IN AN EXPERIMENTAL MODEL OF ACUTE INFLAMMATION IN RATS

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ABSTRACT

In this paper, we studied the effect of diltiazem, a calcium channel blocker, in acute experimental inflammation. The material was represented by 5 groups of rats, which were injected with kaolin solution in one paw. The inflammatory response was measured using a digital plethysmometer in 4 moments: initially, after 1 hour, 2 hours and 24 hours after injection. We compared the obtained values between groups treated with different diltiazem amounts and with the combination diclofenac-diltiazem. Our results show a moderate anti-inflammatory effect of diltiazem in mentioned doses, and also the potentiation of the diclofenac anti-inflammatory effect by the small dose of diltiazem.

Keywords: anti-inflammatory effect, calcium channel blockers, oedema.

4. ERYTHROPOIETIN AND THROMBOCYTOPOIESIS

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ABSTRACT

Erythropoietin (EPO) is a α 1- glycoprotein with a major role in erythropoiesis regulation. EPO also has other roles: antiapoptotic, mitogenic, chemotactic, angiogenic, mobilizer of intracellular calcium, neurotrophic, neuroprotector. Recent researches have shown that EPO has role in diminishing the oxidative stress and inflammation.

Recent data have shown that the treatment with recombinant human erythropoietin (rHuEpo) improves the thrombocyte function in haemodialysis patients, function which is appreciated through the measurement of platelet adhesivity, platelet aggregation and the seric level of the factors implicated in the platelet function. From clinical trials it is also known that the therapy with rHuEpo results in the increase of platelets number.

In this paperwork the authors will follow the erythropoietin's implications in the production of thrombocytes. The experiments were carried out on white Wistar rats in which increased doses of rHuEpo were administered.

From the collected data we have observed an increased platelet number, especially in the 7-th day after the administration of rHuEpo to all groups taken for study. This study comes to confirm the

new data from medical literature according to which erythropoietin could stimulate the production of thrombocytes.

Key words: erythropoietin, thrombocytes, thrombocytosis.

5. EFFECTS OF ZOLPIDEM ON BLOOD GLUCOSE LEVEL, SERUM LIPID CONCENTRATION AND CLOT LYSIS TIME IN NORMOGLYCEMIC AND NORMOLIPIDEMIC RATS

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ABSTRACT

In normoglycemic and normolipidemic rats, the i.p. injection of zolpidem induced an acceleration of fibrinolysis in a dose-dependent bell-shaped manner and various changes of the blood glucose level. Total lipids, total cholesterol and triglyceride serum levels remained unaffected at the dose of 1.25, 2.5 and 15.0 mg/kg, with the exception of the medium dose (5.0 mg/kg) and the next dose (10.0 mg/kg), which lowered them very significantly.

Key words: zolpidem, rats, normoglycemia, normolipidemia, fibrinolysis, serum lipids, blood glucose level, total cholesterol.

6. FOR THE GENERAL PRACTITIONER: THE STUDY OF SOME POLLUTANTS ON THE HEART – IN VITRO AND IN VIVO EXPERIMENTS

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ABSTRACT

Nowadays drinking water and nourishing supplies contain smaller or larger amounts of nitrites, because of industrialization and chemical fertilizers, and these factors are real pollutants that endanger people's health. Taking into account these reasons, we have accomplished a study of nitrites, isonyaside, and gamma picoline, during in vitro experiments performed on 42 isolated frog hearts, and in vivo studies on 28 rats which were EKG monitored. We have noticed that nitrites and especially a mixture of nitrites and isonyaside reduced significantly the amplitude and the contraction intensity of the myocardium with 60% in the in vitro experiments. In vivo studies showed a decrease of cardiac rhythm, associated with bi and trigeminate rhythm, and ischemic T waves, probably due to the formation of a toxic compound, izonicotinoilaside. Pyracetam administration, proved to be wholesome for restarting the normal activity of the heart. We remarked after gamma picoline administration a decrease of the contraction force and amplitude, finally causing cardiac arrest, in both in vitro and in vivo experiments. The administration of PP vitamin proved to be benefic, the heart regaining its normal activity.

Key words: nitrites, isonyaside, gamma picoline, heart, in vitro, in vivo experiment.

7. PROTOCOL FOR ISOLATION AND AUTOLOGUS TRANSPLANTATION OF BETA PANCREATIC CELLS IN PANCREATECTOMIZED PIGS

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ABSTRACT

Transplantation of isolated islets of Langerhans for the treatment of type I diabetes has been developed through experimental research in several animal species, including pigs, and is now being applied to humans with some success albeit limited. Therefore, in the present study, our purpose was to isolate beta pancreatic cells and to demonstrate their efficiency to correct high glucose blood levels in pigs.

In pigs, diabetes was induced by total pancreatectomy and splenectomy. After pancreas removal, its tissue was digested with collagenase and islet purification was performed by centrifugation on discontinuous Ficoll and RPMI solutions. Insulin secreting cells were distinguished using dythizone (DTZ) staining and administered by intravenous injection.

Glycemia was determined for each animal before pancreatectomy and one hour after surgery. We also performed several other determinations in the following days after the surgical intervention.

After a week, in 3 out of 7 pigs, the glucose blood level decreased from initial high values to smaller ones. These results indicate that our procedure for islet isolation could represent an efficient therapeutic method. Moreover, we were able to obtain a large number of viable islet cells, which exhibited the metabolic capacity to correct diabetes.

Key words: diabetes, pancreatectomy, islet cells, collagenase.

8. PRESENT AND FUTURE ANTI-AGING STRATEGIES IN GERONTO-GERIATRICS. 10TH CONGRESS IABG – INTERNATIONAL ASSOCIATION OF BIOMEDICAL GERONTOLOGY, "SENS - STRATEGIES FOR ENGINEERED NEGLIGIBLE SENESCENCE: REASONS WHY GENUINE CONTROL OF AGING MAY BE FORESEEABLE", QUEENS' COLLEGE, CAMBRIDGE, UK, 19-23 SEPTEMBER 2003

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The Congress was opened by **Prof. Denham Harman**, well-known father of "Free radical theory of aging" in 1956, and founder of the IABG (International Association of Biomedical Gerontology) at the 1st IABG Congress in New York, NY, 1985, together with **Dr. Aubrey D.N.J. de Grey**, congress organizer and creator of SENS (Strategies for Engineered Negligible Senescence) concept in October 2000, concept presented in detail at the 9th IABG Congress in Vancouver, Canada, 2001. By their "data presented at this conference", world-wide scientists, contributors from 27 countries, 78 speakers, over 100 poster presenters with their 184 abstracts published in **Biogerontology** (6), show unambiguously "that real anti-aging medicine is not science fiction any more, but science foreseeable" (**A.D.N.J. de Grey**, Abstract no. 44).

The knowledge of molecular and cellular mechanisms implicated in aging and anti-aging processes, in shorting life and longevity, in tissue degeneration and regeneration were presented as starting points in working out of efficient ways in aging control.

Anti-aging strategies will become in a short period of time a revolutionary regenerative medicine by systematic application of biotechnology, bioengineering, nanotechnology and information sciences in the improvement of human health (**W. Haseltine** Keynote Lecture, Abstract no. 74). Therefore, this international debate mainly focused on three anti-senescence strategical fields: aging reversal, aging prevention and deceleration, as well as replacement, repair and regeneration of aged damaged tissue/organ structures.

Epidemiological and demographic implications of aging and anti-aging treated populations, as well as ticklish senescence and prolongevity ethics were discussed.

ELUCIDATION OF AGING MECHANISMS

Many studies and researches were focused on the elucidation and understanding of mechanisms and principles involved in regeneration, longevity, as well as in impairment and aging processes.

A first field refers to animal and human models of premature and accelerated aging. As animal model, SMP 30 knockout (SMP 30 KO) mouse, a mice strain lacking senescence marker protein 30 was presented (**N. Maruyama**, Abstract no. 120). As human model, progeroid Werner's syndrome (WS) was discussed regarding telomeres which may shorten faster in WS fibroblasts (**T. Davis**, Abstract no. 41), defect in WRN

gene, loss of the WRN helicase/exonuclease (**A. M. Rodriguez-Lopez**, Abstract no. 181), abnormal sensitivity to the drug camptothecin, an inhibitor of type I topoisomerase (**J. Lowe**, Abstract no. 50), and relationship between WS fibroblasts and stress-induced premature senescence (**J. P. de Magalhaes**, Abstract no. 116).

The second field is represented by systematic researches in comparative anatomy, biology and zoology, in comparative senescence and biogerontology, investigations which open new prospects in aging control. All five classes of Vertebrata were presented. Zebrafish (*Danio rerio*) has remarkable reproductive and regenerative

abilities and very gradual or sub-negligible senescence in vivo (**S. Kishi**, Abstract no. 95). Also, some species of rockfish (genus *Sebastes*) has negligible senescence. The researches on intra-species fish lifespan comparison (under 30 or exceeding 200 years) conducted to "The Centenarian Species and Rockfish Project", which has a total of 14 pilot studies (**J. C. Guerin**, Abstract no. 70). Tailed amphibians (newts and salamanders) possess strong regenerative abilities, being depended on the local activation of plasticity in residual differentiated cells (**J. P. Brockes**, Abstract no. 18). Also, turtles (reptiles of the order Chelonia, comprising aquatic and terrestrial species) represent naturally long-lived animal models for the study of longevity and slow aging (**D. J. Holmes**, Abstract no. 79). In birds, telomerase profiles vary with lifespan. The two short-lived species (zebra finches and tree swallows) have high telomerase activity with a sharp down-regulation in both the young and old adults), but the two long-lived species (common terns and storm-petrels) have relatively high telomerase activity, that did not differ in the three age-classes (hatchling, young adult and old adult), (**M. F. Haussmann**, Abstract no. 75). Within-individual selection of efficient mitochondria, due to selective pressure created by the high energetic demands of flight, determines the maximum lifespan potential (MLSP) of 34 years at bats - flying mammals, little brown bat (*Myotis lucifugus*) in comparison with MLSP of 2 years at short-tailed shrews, mouse-like insectivore mammals (*Blarina brevicauda*), (**A. K. Brunet-Rossini**, Abstract no. 20).

The third field of studies pointed out the mitochondria and oxidative stress parts in biogerontology, aging progressing and pathology. In this respect, the oxidative stress/antioxidant defence gene network investigation (**R. Arking**, Abstract no. 7), mitochondrial reactive oxygen species' production correlated with lifespan of mammals (**G. Barja**, Abstract no. 11), and non-invasive human oxidative stress profiling, combining both oxidative damage impacts with defence/repair processes (**R. G. Cutler**, Abstract no. 39) become useful search tools. In the brain, cytochrome oxidase (COX), the terminal enzyme of the mitochondrial respiratory chain, can be considered a reliable index of the mitochondrial metabolic competence (**C. Bertoni-Freddari**, Abstract no. 14), and its activity can be taken into account as an endogenous marker of neuronal oxidative metabolism (**C. Bertoni-Freddari**, Abstract no. 15) which is modified with age. In Alzheimer's disease (AD), both lesions (amyloid-beta and tau, the major components of senile plaques and respectively neurofibrillary tangles) occur as a consequence of oxidative stress and are relatively late events

(**M. A. Smith**, Abstract no. 155). Correlation between lipofuscin accumulation, imperfect autophagic recycling, oxidative stress and mitochondrial damage was studied in aging of cultured rat cardiac myocytes (**A. Terman**, Abstract no. 21, **A. Terman**, Abstract no. 162). In addition, at the transcriptional level, there is an age-related impairment of specific inducible pathways in the response to oxidative stress in the mouse heart (**M. Edwards**, Abstract no. 138). The phenotypic expression of age-associated mtDNA deletion mutations in rat skeletal muscle is fiber type-dependent (**J. W. Pak**, Abstract no. 132), rat muscle protein, phosphorylase B from Fischer 344 rats undergo oxidative and nitrative modifications under normal biological aging conditions (**V. S. Sharov**, Abstract no. 151), and skeletal muscle atrophy from immobilization and aging is the result of activation of both intra- and extracellular proteolytic systems (**A. Z. Reznick**, Abstract no. 142). Also, mitochondrial respiratory function in culture senescent fibroblasts (**E. Huetter**, Abstract no. 84), oxidative stress in prostate fibroblasts (**R. Gander**, Abstract no. 58), as well as oxidative stress during replicative senescence of human peritoneal mesothelial cells (**K. Ksiazek**, Abstract no. 106) were presented. **K. J. A. Davies** (Abstract no. 40) described and discussed on the two different patterns of proteolytic activity decreases with age: Proteasome (found in cytoplasm and nucleus) and Lon protease (from mitochondrial matrix). Non-metal and metal toxic compounds were investigated in relation with oxidative stress, aging and neurodegeneration: kainic acid (**Z. Chen**, Abstract no. 29), aluminium (**P. Fattoretti**, Abstract no. 51), and iron (**D. W. Killilea**, Abstract no. 92, **T. Kurz**, Abstract no. 107).

REAL AGING REVERSAL STRATEGIES.

The first direction is genetic manipulation in mouse (**M. R. Capecchi** Keynote Lecture, Abstract no. 24) to create the Methuselah mouse (**D. Gobel**, Abstract no. 62). Then, in this century, the results can be applied in human longevity medicine, to obtain Methuselah's (an antediluvian patriarch - Genesis, 5:27) lifespan of 969 years. Because sarcopenia (loss of muscle mass and function) is one of the most marked problems associated with aging and health care systems, its amelioration using mechano growth factor (MGF) delivered as a peptide or by gene therapy acquires new dimensions (**G. Goldspink**, Abstract no. 63). The identification of human genes prolonging lifespan by a high-throughput functional genomic strategy (**C. Chen**, Abstract no. 28) becomes necessary.

Given the recent technical developments of telomere dynamics, that is, quantitative telomere fluorescence in situ hybridisation (Q-FISH) and PCR based single telomere length analysis (STELA), (**D. M. Baird**, Abstract no. 10), the second type of intervention for aging reversal addresses telomere erosion with age, by telomerase activation through transcriptional control of telomerase reverse transcriptase (hTERT), (**J. W. Shay**, Abstract no. 152, **E. Trivier**, Abstract no. 166), or by a telomerase-independent mechanism (**D. Broccoli**, Abstract no. 17). In addition, interference with the action of DNA damage checkpoint kinases can restore the DNA replicative ability of senescent cells (**F. d'Adda di Fagagna**, Abstract no. 49). On the other hand, the formation of 8-oxodG at the GGG triplet in telomere sequence induced by oxidative stress could participate in acceleration of telomere shortening (**S. Kawanishi**, Abstract no. 87). Because telomeres may shorten faster in Werner's syndrome (WS) fibroblasts (**T. Davis**, Abstract no. 41), telomere manipulation can be useful in this inherited genetic

disease. Moreover, telomere biology plays a causal role in normal human aging, as well as in age-related diseases, including cancer. Therefore, specific interventions in oncology (i.e., telomerase vaccines, telomerase inhibitors and telomerase promoter-driven cell killing) open new therapeutic expectations (**C. B. Harley**, Abstract no. 71). Also, as an anti-cancer strategy, telomere dynamics may be efficient in combination with stem cell utilizations, the so-called WILT (Whole-body Interdiction of Lengthening of Telomeres) therapy (**A. D. N. J. de Grey**, Abstract no. 43). Gene therapy of virus-specific CD8 T cells with the catalytic component of telomerase (hTERT) corrects many of cell cycle-related defects, and leads to telomere maintenance and restoration of anti-viral cytotoxic functions (**R. B. Effros**, Abstract no. 48).

The third aging reversal intervention is transgenic introduction of microbial hydrolases from the genus *Rhodococcus* into human postmitotic cells and organs to destroy subcellular lipofuscin/age

pigment aggregates and recalcitrant components of atherosclerotic plaques from arteries (**J. A. C. Archer**, Abstract no. 5).

AGING PREVENTION AND DECELERATION THERAPIES

The first orientation in this field of strategies is Caloric Restriction (CR), the world-wide tested and accepted intervention to extend lifespan and to retard the age-related declines in mammalian structures and functions. Theoretical considerations and the mechanism of calorie/aging-rate interactions were presented by **R. M. Anson** (Abstract no. 4). **G. Barja's** research demonstrated that long-lived homeothermic vertebrates, CR rodents and long-lived Ames dwarf mice have lower rates of mitochondrial reactive oxygen species (ROS) production and lower levels of mtDNA oxidative damage (Abstract no. 11). **N. Barzilai** et al. have shown the potential role of hexosamine biosynthesis pathway (HBP) on the mechanisms mediating the beneficial effects of CR (Abstract no. 12). Life-long CR has been shown to have neuroprotective effects, as well as to prevent age-associated loss of skeletal muscle fibres in Fischer-344 rats (**C. Leeuwenburgh**, Abstract no. 110), and of skeletal muscle fibres in Rhesus monkeys (**S. M. McKiernan**, Abstract no. 121). In addition, the positive influence of CR on insulin/IGF-1 signaling (IS) pathway (**M. Zhu**, Abstract no. 177) and on mtDNA deletion decrease (**P. Cassano**, Abstract no. 179) were presented.

As CR is unpleasant and restrictive for humans, studies with CR mimetics (drugs mimicking the gene expression effects of CR) gain ground as a prolongevity strategy (**D. K. Ingram**, Abstract no. 81, **S. R. Spindler**, Abstract no. 156).

The second type of intervention in aging prevention and deceleration is by regular physical activity. Regular exercise induced adaptive molecular responses even at old ages and reduced age-related increase in inflammatory and other detrimental consequences caused by oxidative stress (**S. Goto**, Abstract no. 67) in the brain, cardiac and skeletal muscles. Moreover, exercise induced cardioprotection against ischemia-reperfusion (I-R) injury (**S. K. Powers**, Abstract no. 136), and attenuation of osteoporosis (**K. Kikkawa**, Abstract no. 91). Combination of physical activity with antioxidant protection (North American ginseng - Panax Quinquefolium or an oat antioxidant - avenanthramides) via dietary supplementation (**L. L. Ji**, Abstract no. 85), or with metabolic therapy (coenzyme Q10, alpha-lipoic acid, magnesium orotate and omega-3-fatty acids) and mental relaxation and stress reduction, such as Metabolic, Physical and Mental (MPM) program (**F. L. Rosenfeldt**, Abstract no. 145) has positive effects on skeletal muscles and myocardium, respectively in cardiac surgery.

The third possibility is represented by daily mental training in a complex, enriched environment, which has positive effects on exploration, cognitive performances and motor activity in aged rats (**C. I. Fernandez**, Abstract no. 54).

The fourth strategy to aging prevention and deceleration is the use of nutri-ceuticals and/or metabolic pharmaceuticals with high specific anti-aging actions and properties.

Dietary supplementation with polyphenol-rich fruits (blueberries) increased neurogenesis and improved cognitive performance (**J. A. Joseph**, Abstract no. 86), and with tetrahydrocurcumin (biotransformed metabolite contained in turmeric of Indian curry) or green tea polyphenols significantly rised lifespan (**K. Kitani**, Abstract no. 96).

Also, dietary carnosine (b-alanyl-L-histidine) increased lifespan (**G. Gallant**, Abstract no. 57), and dietary intake of omega-3 PUFA (polyunsaturated fatty acid) and coenzyme Q10 counteracted age-related alterations of heart cell and mitochondrial membranes (**S. Pepe**, Abstract no. 135).

Metabolic pharmaceuticals and anti-aging medicines have beneficial actions and effects on human longevity (**S. V. Ukraintseva**, Abstract no. 168), in geriatrics and age-related and degenerative diseases. Alpha-lipoic acid enhances sodium potassium ATPase activity and reduces lipofuscin accumulation in several brain regions (**P. Arivazhagan**, Abstract no. 6), while alpha-lipoic acid and acetyl carnitine restore mitochondrial functions (**B. N. Ames** Keynote Lecture, Abstract. no. 3). Both aging and vitamin E deficiency are responsible of altered RNA pathways in hepatocytes (**M. Malatesta**, Abstract no. 117), and of marked decrease of MAP-2 level (protein involved in dendritic remodeling) in hippocampus (**T. Casoli**, Abstract no. 27). In addition, the long-term treatment with CDP-Choline (precursor of phosphatidylcholine with repairing actions on brain membranes) has

positive effects of hippocampal morphology, as well as on memory and behaviour (**D. Crespo**, Abstract no. 38). Moreover, the administration of a synergistic biological therapy, with new cell-trophic-regenerative and antioxidative-neurometabolic-cerebrovascular actions, has demonstrated its concomitant preclinical - experimental efficacy in distress, impairment and aging (**D. Riga, S. Riga, F. Schneider**, Abstract no. 143), as well as its clinical - human efficiency in distress, geriatrics and related diseases (**S. Riga, D. Riga, F. Schneider**, Abstract no. 144). This advanced prophylactical and therapeutical anti-stress and anti-aging strategy was world-wide patented (1994-2003 in 25 countries). Interesting results were reported with a lipid algae extract (*Phaeodactylum tricorutum*) that has a stimulating and/or protective effect on proteasome in culture human keratinocytes and in stratum corneum skin cells (**C. Nizard**, Abstract no. 128), and with a plant extract (*Salix Alba*) on heat shock protein (HSP) 47 in aged, photo-aged and senescent normal human fibroblasts (**E. Noblesse**, Abstract no. 129). Because zinc-bound-metallothionein in the marker upstream affecting functional biochemical cascade involved in immune plasticity maintenance, zinc supplementation has beneficial effects in old infected patients (**E. Mocchegiani**, Abstract no. 124).

The fifth direction is on immune system, system strong impaired by mammal aging. Thus, therapeutic intervention with interleukin (IL)-7 in old mice increases both the size of the thymus and its subsequent output benefiting the functional performance of the T cells in the peripheral T cell pool (**R. Aspinall**, Abstract no. 8), and the creation of a CCR9/IL-7 fusion protein reduces dosage levels and treatment frequency (**S. M. Henson**, Abstract no. 77). On the other hand, the immunization (antibodies) against beta-amiloid can slow cognitive decline in patients with Alzheimer's disease (**R. M. Nitsch**, Abstract no. 127).

The sixth strategy is represented by other new approaches of anti-aging mechanisms. Thus, repetitive mild heat stress has numerous anti-aging hormetic effects: maintenance of stress protein profile, reduction in the accumulation of oxidatively and glycooxidatively damaged proteins, stimulation of the proteasomal activities for the degradation of abnormal proteins, improved cellular resistance to severe stressors and enhanced levels of various antioxidant enzymes (**S. I. S. Rattan**, Abstract no. 140). On the other hand, the gatekeeper molecules, represented by caveolin, play the prime roles in the senescent phenotypes (**S. C. Park**, Abstract no. 133), and the reduction of caveolin-1 in senescent fibroblasts restores the normal growth factor responses and recovers the mitogenic signaling (**K. A. Cho**, Abstract no. 33).

TISSUE ENGINEERING - REGENERATIVE MEDICINE STRATEGIES

The three R's of regenerative medicine (Replace, Repair and Regenerate) are very actual and necessary in the next years, because at present aged populations have need of immediate solutions for damaged or failed tissue/organ structures. For these is no time for aging prevention, but is the time for organ reparation and/or replacement. Therefore, the development of regenerative medicine (the older term - tissue engineering) becomes imperative (**M. V. Sefton**, Abstract no. 150), as well as the extensive use and unlimited supply of cells, soluble and matrix bound factors and supporting structures to regenerate/replace aged/damaged tissue/organ structures and functions are the rational solutions.

In this field, research and characterization of stem cells are very important and timely: aging of stem cells in general and of hematopoietic stem cells in particular (**G. van Zant**, Abstract no. 173), role of mitochondrial mutations in aging of intestinal stem cells (**T. B. L. Kirkwood**, Abstract no. 94), opportunities to transform human embryonic stem cells into young cells in vitro for therapy (transplant) in age-related diseases (**M. West** Keynote Lecture, Abstract no. 175), and relationship between stem cells and carcinogenesis (**M. D. Lynch**, Abstract no. 115).

Supplemental growth factors can amplify the local stimulus of injury or degeneration by mobilizing uncommitted stem cells to target and rebuild damaged tissues (**N. Rosenthal**, Abstract no. 146). In addition, rat femur bone marrow stem cells graft to striatum and hippocampus of impaired aged rats generated a significant functional recovery (**C. I. Fernandez**, Abstract no. 53), and combining stem and gene therapy in aging brain with Parkinson's disease also brought about important restoration (**C. Svendsen**, Abstract no. 159).

For humans with unsolved mortal diseases also there is a solution with a bridge to a time in which senescence will be controlled: cryobiology with medical time travel (**J. B. Lemler**, Abstract no. 111).

EPIDEMIOLOGY, DEMOGRAPHY AND ETICS

Demographic and epidemiological studies on human supercentenarian (**L. S. Coles**, Abstract no. 34), delay and/or escape of cardiovascular disease in centenarian offspring (**D. F. Terry**, Abstract no. 163), pathways to exceptional human longevity (**L. S. Corder**, Abstract no. 36), gender differences in Alzheimer's disease neuropathology

(**E. H. Corder**, Abstract no. 35), obesity, infectious diseases and forecasts of human life expectancy (**S. J. Olshansky**, Abstract no. 131), and Belfast Elderly Longitudinal Free-living aging study (BELFAST), (**I. M. Rea**, Abstract no. 141, **O. A. Ross**, Abstract no. 147) were presented.

Debates on immortal ethics (**J. Harris** Inaugural SENS Lecture, Abstract no. 73), social, political and ethical obstacles to human life extension (**S. N. Austad**, Abstract no. 9, **A. Caplan** Keynote Lecture, Abstract no. 25, **J. K. Davis**, Abstract no. 42) and planning for demographic changes (**G. Stock**, Abstract no. 157) become topical, because now prolongevity and regenerative medicines are certainties.

By extensive scientific participation, discussions and debates, the 10th IABG Congress gave life, implemented and determined the scientists to reason, to research and to work with the SENS concept in redefining of interventional strategies on aging processes.

Thus, this congress may be considered as "SENS 4" (**A.D.N.J. de Grey**), and as international acceptance and devotion of this concept. Indeed, **SENS earned world-wide SENSE** in global scientific community, and this is to A.D.N.J. de Grey's great merit and effort.

At beginning of century, this congress, with the main papers published as a volume of the prestigious *Annals of the New York Academy of Sciences* (2), together with the recent five monographs (1, 3, 4, 5, 7) of new book series "Biology of Aging and its Modulation" (General editor S.I.S. Rattan), which develop important themes of the congress, represent the task force in the advance of biogerontology.

P.S.

Punting on the Cam (river which passes through Cambridge, near Queen's College), the last meeting event on September 23th, 2003, was the first congress-related practical demonstration of right use of daily physical activity in aging prevention and deceleration.

Caloric restriction mimetics become of great prospects taking into account the large appetite of participants, especially on English dishes.

In addition, the congress was a strong and practical example of cerebral activation (mental training) in a complex and enriched place (distinguished scientists in a charming environment).

REFERENCES

1. Aspinall R. *Aging of Organs and Systems*. Dordrecht, NL, Kluwer Acad. Publ., 2003.
2. de Grey A.D.N.J. Ed. *Strategies for Engineered Negligible Senescence Why Genuine Control of Aging May Be Foreseeable*, Ann. New York Acad. Sci., vol. 1019. New York, NY, New York Academy of Sciences, 2004.
3. Kaul S.C., Wadhwa R. Eds. *Aging of Cells in and Outside the Body*. Dordrecht, NL, Kluwer Acad. Publ., 2003.
4. Osiewacz H.D. Ed. *Aging of Organisms*. Dordrecht, NL, Kluwer Acad. Publ., 2003.
5. Rattan S.I.S. Ed. *Modulating Aging and Longevity*. Dordrecht, NL, Kluwer Acad. Publ., 2003.
6. Rattan S.I.S., de Grey A.D.N.J. Eds. Abstracts of the International Association of Biomedical Gerontology 10th Congress, Cambridge, UK, 19-23 September 2003. *Biogerontology* 2003; 4 (Suppl. 1): i-xxi, 1-107.
7. von Zglinicki T. Ed. *Aging at the Molecular Level*. Dordrecht, NL, Kluwer Acad. Publ., 2003.

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