1-2 February 2010
KORANET PARTNERING EVENT

Research for life-long health

Çimen KARASU, Ph.D.

Professor in Medical Pharmacology
Gazi University, Faculty of Medicine, Ankara
Leader of the "Antioxidants in Diabetes-Induced Complications (ADIC) Study Group"
Head of the "Cellular Stress Response and Signal Transduction Research Laboratory"
President of Turkish Anti-Aging Society A3MST
ESAAM Board Member, WAAAM Advisory Board Member

Diabetes as a model of glycoxidative aging: Potential Medical Remedies by Natural and Synthetic Antioxidants

RESEARCH FACILITIES

"Cellular Stress Response and Signal Transduction Research Laboratory"
Faculty of Medicine, Gazi University
"Antioxidants in Diabetes-Induced Complications (ADIC) Study Group"

1. To Search Potential Therapeutic Chemicals and Compounds

A- Design and chemical synthesis of some substituted pyridoindoles (Antioxidant, ALR2 inhibitory activity, glycation inhibitors).

B- Evaluation of the novel synthetic derivatives in vitro: Structure elucidation; physico-chemical properties, acidobasic behavior, lipophility and biological availability characterization; antiglycation, antioxidant and ALR2 inhibitory activity in model systems in vitro.

C- Development of some plant material (e.g. leaf and fruit extracts, seed oils): extraction, standardization,lyophilisation and other analysis.

RESEARCH FACILITIES

"Cellular Stress Response and Signal Transduction Research Laboratory"
"Antioxidants in Diabetes-Induced Complications (ADIC) Study Group"

2. **Cel Culture Studies:** Standard laboratory equipment to perform specialized molecular biological and biochemical analysis, assays for cell differentiation, characterization, markers for senescence, aging, apoptotic signal transduction, glycoxidative stres markers, calcium homeostasis, endoplasmic reticulum and mithocondria stresses, insulin signaling. Micro plate reader, ELISA, spectroscopy, luminometer, western blotting, real time PCR, histological staining, immuno-staining, magnetic resonance spectroscopy for animals, fluorescence and electron microscopy.

A- Cell Lines: INS-1E, rat cardiomyocytes, rat vascular smooth muscle, mastocytoma, HT22 neuronal cells.

B- Isolated cell systems: Islet beta-cells, mouse cardiomyocytes

RESEARCH FACILITIES

"Cellular Stress Response and Signal Transduction Research Laboratory"
"Antioxidants in Diabetes-Induced Complications (ADIC) Study Group"

3. **Experimental Animal Models:** Diabetes, Hypertension, Hypercholesterolemia, inflamation and others.

   Treatment with natural or synthetic compounds.

A- Evaluation of metabolic and general characteristic, hemodynamic parameters, blood biochemistry and tissue biochemistry.

B- Isolated tissue experiments:

   a. Responsiveness and Contractility: aorta, m.artery, siciatic nerve, vas def. papillary musc. atria, whole hearth

   b. Tissue structure and morphology

THE FACTS

The formation of advanced glycation end-products (AGEs) progressively increases with normal aging, even in the absence of disease. However, they are formed at accelerated rates in diabetes due to uncontrolled hyperglycemia. In the presence of uncontrolled hyperglycemia, the increased AGEs production and other multiple pathways mediate the generation of RONS leading to cellular redox imbalance. Increased AGEs and RONS are the major reasons for increased cellular stress responses and the injury. Chronic hyperglycemia has been shown to be involved in β-cell dysfunction, a phenomenon known as glucotoxicity. AGEs and RONS are not only markers but also important causative factors for the pathogenesis of diabetes induction and the progression of its complications due to glycoxidative stress. Unmitigated glycoxidative stress can lead to a decrease in cellular longevity.

PROJECT IDEA

The strategies involving the treatment with natural and synthetic antioxidative agents and their combination with other AGE inhibitors suggest the promising means of therapy to prevent the pro-oxidant feature of diabetes, to protect redox status of the cells, to slow down aging mechanisms and to delay the progression of diabetic complications.

MAIN OBJECTIVE

The main objective is to investigate the effects of natural (e.g.pomegranate seed oil) and/or synthetic (e.g. pyridoindole compounds) glucoxidative stress inhibitors in cellular metabolism (calcium homeostasis mytochondria function), signal transduction (apoptosis) and tissue functions and structure.

OUTCOMES

The project comprises a multidisciplinary approach to the investigation of molecular factors in the generation and the etiology of chronic diabetic complications.

The evaluation the effects of some natural or synthetic antiglycation agents, antioxidants and/or aldose reductase inhibitors may provide closer insights into the molecular mechanisms of glucose toxicity and give information useful for developing new therapeutic strategies for the treatment of diabetes.

EXPERTISE

Experimental approaches:

Advnced preclinical studies

- **Cell culture studies:** Induction of glucotoxicity; apoptotic models; calcium homeostasis, proteosome activity, glycoxidative stress markers, inflammaging marker; expression of the stress signaling molecules. INS1E cell line:insulin releasing. Skin fibroblasts:Skin aging
- **Animal studies:** The Main Experimental Animal Groups:
  Young and old diabetic and non-diabetic rats treated or untreated by individual potential therapeutic compounds or therapeutic compounds combinations.
  Metabolic, biochemical, functional and morphological studies in blood, isolated cells and isolated different tissues. Glycoxidation, lipoxidation and nitrosation markers.
  Isolated tissue studies.

PARTNER SOUGHT

- The requested partner should be qualified in cellular mechanisms of age-related metabolic diseases such as diabetes and knowledge on drug target related with glycoxidative stress, and drug design and phytotherapeutics.
- The studies on cellular signal transduction systems, the facilities on genetically diabetic rats, isolated rat pancreas beta cells, and the trying the effects of potential drugs on diabetic patients (clinical studies) are open to collaborations.

ANOTHER APROACHMENT

- Another Project proposal: A network of excellence between Aging, AntiAging and Longevity organizations.
- Purpose: Strengthening and advancing scientific and technological excellence in the area of healthy aging.
- Expected Impact: To bring scientists and health professionals together in order to discuss the medical therapeutic novelties, social and economic dimensions of aging and formulate solutions over the long term.
- KORANET SCIENTIST can discuss and improve the project in order to offer FP7 for the 2011 calls.

CONTACT DETAILS

Prof. Çimen KARASU

Gazi University, Faculty of Medicinei, Department of Medical Pharmacology, 06500, Besevler, Ankara, Turkiye.

karasu@gazi.edu.tr, cimenkrs@gmail.com, +90 532 7467148, +90 312 2026921

Our Present Partners are: