FP7 Cooperation Work Program:
Abstract for partner search to the National Center of Therapy

About the Company

The National Center of Therapy, Tbilisi, Georgia (NCT) provides clinical based research measures in different fields: Cardiomyopathies (Dilated, Hypertrophic), Atherosclerosis and Ischemic Heart disease, Geriatry and Drug Clinical Trails for (stage III and IV). NCT was founded by Academician Nodar N. Kiphshidze as the Insitute of Clinical and Experimental Therapy (internal medicine) at the time of Former Soviet Union in 1961. The decades it provided large-scale of basic and applied scientific research in different thematic areas of internal medicine and common non-communicable diseases. Currently, NCT, as the scientific research center functions in the system of Georgian National Academy of Science. Despite of difficulties in provision of basic science researches NCT preserved and developed research infrastructure for clinical investigations in above named fields.

Research Focus

NCT developed the clinical based protocol and releted methods of clinical investigations for contemporary screening and risk stratification of Familial Hypertrophic Cardiomiopathy.

Current interest for research activities is releted to novel signalling proteins those may link molecular bridge between the genetic defects and phenotype of hypertrophic cardiomyopathy.

Latest research findings from animal models provide evidences to implicate aldosterone in the pathogenesis of cardiac hypertrophy, fibrosis, and disarray in HCM, including elevated myocardial aldosterone and aldosterone synthase mRNA levels in HCM.

Blockade of MRs in a genetically engineered mouse model of HCM mutation normalized myocardial collagen content and attenuated myocyte disarray, phenotypes associated with SCD and heart failure in HCM and improvement in diastolic function. Evidences implicate that impaired N-cadherin–mediated myocyte-myocyte attachment, as a consequence of phosphorylation of bcatenin, in the pathogenesis of myocyte disarray, the hallmark of HCM.

Spironolactone (the blocker of MRs) restores b-catenin–N-cadherin complexion cellular distribution of N-cadherin and reduced myocyte disarray and fibrosis. These results identify aldosterone as a fundamental molecular link between sarcomere gene mutations and cardiac phenotypes in HCM.

Additionally, earlier clinical investigations of chronic heart failure caused by ischemic heart disease and dilated cardiomyopathy could provide evidences that of MR blockade with spironolactone affects molecular substrates of myocardial fibrosis and reduces cardiovascular mortality and morbidity.

Suggesting over-expression of MRs as the fundamental molecular link between sarcomere gene mutations and phenotypes in HCM the results of investigations on animal models illustrate the need for clinical studies in humans to determine the role of aldosterone on clinical phenotypes of the disease. Clinical testing of this hypothesis may valuably contribute to clear up of potential beneficial effects of MR blockade in HCM.

Current Capacities and Expertise

Scientific research activities of human HCM in NCT comes from early 80_{th} of last century. In pair with investigations of dilated cardiomyopathy, research activities for studying of pathogenesis, profile of clinical manifestation and risk prediction was developed. Main of immune-genetics aspects of myocardium hypertrophy

(HLA profiles in Georgian population), expression and distribution of hypertrophy in myocardium, risk prediction and profiles of clinical phenotype of familial forms of HCM was investigated.
Results of these activities have given capabilities for development of the clinical based protocol for contemporary screening and risk stratification of HCM. During last years the protocol and releted methods of clinical investigations are currently applied in NCT. More than 60 patients were undergone with it.
Earlier, in 90th, NCT provide clinical investigations for exproling of reninangiotenzine- aldosterone system activity in dilated cardiomyopathy and heart failure. Research findings from these are regularly published.
NCT has access to extensive expertise within clinical medicine (cardiology), cardiac imeging (echo, radiology), biochemistry and immunology. From early 80th of last century the specialized department of cardiomyopathy reaserch, with clinical facility is functioning in NCT. It is staffed with experienced researchers skilled in clinical investigations of cardiomyopathies.
NCT has close collaboration with other relevant research institutions of Georgian Academy of Sciences, university centers, health providers and professional associations.

Plans and Intentions

Based on substantial background and current capacities NCT develops its current research activities for human HCM study in some directions:
1. Create of an simple institution based registry of HCM patients thought the country (Georgia) and region (South Caucasus - Azerbaijan and Armenia), using of data of existing contemporary screening protocol (including family history, trait of inheritance, morphological and clinical phenotype and risk assessment). This can provide substantial amount of data for human HCM research and clinical medicine
2. Develop research activities for testing the role of increased aldosterone occupancy of MRs in phenotype of HCM through the investigation of aldosterone exposure and expression of molecular markers of myocardium hypertrophy and fibrosis.
3. Explore the possible bridges between the genetic substrate of HCM and exposure of aldosterone on MRs.
4. Strength the existing research capacity in molecular medicine and implement professional education tools for HCM study using the new scientific developments.

FP7 partnering

NCT seeks partners and expects to get the research consortium for participation in FP7 program: Health 2010. We have knowledge and expertise to contribute to projects within the following calls:

- HEALTH.2010.1.1-1. Harmonisation of phenotyping and biosampling for human large-scale research biobanks;
- HEALTH.2010.1.1-2. Genomics and Genetic Epidemiology of Multifactorial Diseases;
- HEALTH.2010.1.2-1. Tools for the identification and the detection of biomarkers in clinical samples and patients;
- HEALTH.2010.1.2-2. Stratification approaches and methodologies to select from a wide range of biomarkers relevant candidates for clinical validation;
- HEALTH.2010.1.2-3. Harmonization, validation and standardisation in genetic testing;
- HEALTH.2010.2.1.1-2. Coordination action(s) on standards in large scale data gathering;
- HEALTH.2010.2.4.4-2. ERA-Net on rare diseases;

For further information about our research and expertise, do not hesitate to contact us. We are welcoming discussions about any project proposals and consortium ideas.

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