Abstract

The real challenge in Serbia is combating both vascular diseases and diabetes, being common diseases, both multigenic and multifactorial ones. Thus, we organized project as complex one with working groups divided by topics related to type of both disease and environmental exposure, followed by ethical and lifestyle aspect too. The questions are: 1) if the environmental exposure is equal for individuals within some population group why they suffered different diseases or if they are from different population groups why frequency of same disease is different?, and b) if the genomic structure of certain either individuals or population groups is a very similar, why they suffered different diseases? To get the right answers for both questions, we have to achieve right data for both genomic structure and environmental exposure within chosen different local entities. By well organized systematical research of collaborators from different fields supported by modern technology (bio-, nano- and ICT), geneticists, cell biologists, clinicians, bioinformaticists, physicists, chemists, will apply their experience and the latest worldwide knowledge combining applied and basic research, with output including data bases, risk assessment, development of diagnostic and therapeutic tools, and better knowledge of gene-environment interaction. Principal users will be ministries of health and env. protection, some oil, mining, food and pharmaceutical companies.

Keywords

CVD, diabetes, gene/environment interaction, risk assessment, biomarkers, biosensor

Expected key results

1. Identification of gene variations responsible for susceptibility for the diseases examined in the particular region:
   • variations in genes involved in inflammation
   • variations in genes involved in glucose/lipid metabolism and blood pressure regulation
   • variations in genes involved in specific metabolic pathways of examined environmental agents (heavy metals, etc)

2. Causality of seasonal frequency of rupture of abdominal aorta aneurism

3. Impact teeth hygiene on vascular disease

4. Identifying priority list of pollutants that may contribute to reduced health of selected population groups.
•Proposing enhancing of regular monitoring of environmental pollutants and quality control of consumer products and food to be usable for integrated assessment of exposure of population to particular chemical agent.

5. Data base on geographical distribution of indoor Rn concentration regarding selected areas of Serbia

•Estimate Rn exposure of chosen population – contribution to the National Rn program

•Contribution to the European Atlas of Rn mapping

6. New nutritional and lifestyle questionnaire standard form.

7. Simple assay kit for measuring NOS activity in different pathophysiological conditions including adults with metabolic syndrome.

8. Chip and efficient biosensor for detection of variations in DNA

**Research relevance**

We offer a new concept of systematic health survey with molecular approach of environmental exposure of humans connected with clinical practice using modern technology opportunities. This approach should be important as an intermediate step from general risk assumption to personalized one which is still a great desire. It will bring new models in sense of diagnostic, therapeutic and prevention tools. Amazing bio-monitoring opportunities confront expert beliefs, regulatory concepts and responsibilities in health care and are opening new perspective for multi-factorial epidemiology. For example, a dose as unique risk indicator is no longer self-evident. A number of metabolic pathways serving either for normal function cells, tissues or organs or as an answer to environmental constant or incidentally generated agents depend of existing target genetic structure. Connecting all results as data bases from different sources (investigations) should give us a novel knowledge of gene-environment interactions and new standards for questionnaires, diagnosis, monitoring of health/environment status and therapy. Another practical benefit of this project should be personalized recommendation of dietary consumption and commercial test-kit of NOS activity as routine test before physician’s decision in particular cases. Development the simple, rapid and accurate assay kit for determination of NOS activity will provide an extremely powerful tool in diagnostic and therapy of various pathophysiological conditions such as: diabetes, cardiovascular and obesity disease as well as inflammation. Furthermore, by developing this assay kit we may be able to design therapeutic strategies to reduce cardiac dysfunction and tissue injury in ischemia, infraction, diabetes and obesity. In addition, the prevention of the overproduction of NO in the living organism trough control of regulatory pathways may assist in the treatment of high NO-mediated disorders without changing physiological levels of NO. Proposed working out of new standard questionnaire should bring data more directly applicable as parameters of future risk assessment for the diseases. The genomic characterization of chosen population groups as key parameter will be of great interest. The proposed work on nano-based biosensor for analysis of gene variations will be tested by genomics group in our
effort to bring high sophisticated technology for both more sensitive and low cost effective analytical method. Chemicals are indispensable part of the contemporary life. They enable enormous benefits for population such there are contained in pharmaceuticals, cosmetics, used for food safety, contribute that textile and consumer products are more attractive, etc... At the other side in numerous situation levels of chemicals in air, water, soil, consumer products and food may persist risk for human health. To know if chemical perform benefit of risk it is essential to perform comprehensive scientific and technical expertise and assessment. New methodologies of integrated assessment have been carried out through ongoing FP6 and FP7 project related to environment and health topics, in which participation of researchers from Serbia is still limited. Case studies that will be performing through this project will be done using contemporary tools, including available analytical methods and software’s. On the examples that reflect our country we will obtain response about level of risk of exposure for chosen scenarios and chemicals. Also, members of the public are concerned with low daily irradiation not only regarding natural radiation, but also in the context of environmental releases from industrial places. Thus human exposure can be measured either in normal residential condition or at the occupational level. By radioactive disintegration of uranium and thorium, different isotopes of radon arise, being alpha emitters. Inhalation of alpha particles and dose risk assessment has its need and relevance in the fact that it constitutes the main irradiation of a general public. It is distributed over the whole life as a chronic airborne pollutant able to reach a large number of target cells. As radon has been identified as an important radiological hazard, large efforts have been made in many countries to map indoor radon concentrations levels. The important proposed task is definition of the working variable “indoor radon concentration”, the understanding of “longitudinal” variability in Rn concentration at one point and the proper definition of a geostatistical variable “Rn concentration”. However, new relevant data emerging from ongoing research have a potential impact on public health in situation involving a risk from exposure to for example radiation, regarding the risk of radiation induced circulatory diseases. This requires new approach in methodology and successful collaboration with local communities, which are based on sociological partnership innovations, mutual respect and consideration of distributive justice in decision making. Teaching the people on radioactive environment in which we live with from the very beginning the “radiofobia” phenomena is avoided. Our scientific progress in these fields needs a new trans-disciplinary framing of complexity where social sciences and humanities are more active involved to complete scientific insight. In that sense, good experience of radon group in the project will be applied to genetic testing, dietary consumption, cultural (ethnicity, gender) and socioeconomic matter. The objective diseases, resulting in serious health, social, economic and political consequences, deserve the great attention in direction to reduce them in next decade. The country policy makers, as ministries of health and environment protection should be the principal users of the project results, then local authorities, other researchers, as well as some industrial companies (mining, oil, electric power, pharmaceutical, food).

Relationship between basic and applied research

The proposed basic research should be directed to the impact of genomic variations to either normal function of cells, tissue or organs or specific environmental agents’ metabolism. The key molecules or processes should be defined as specific biomarkers for the health status and/or diseases.
Full clinical characterization of health status of either an individual or particular group of individuals should contain not only symptomatic parameters or disease history but also their genetic, nutritional, habitat and socioeconomic status parameters. The clinical investigations in the proposed project will try to incorporate results of basic research of other groups to standard diagnostic and therapeutic procedures or recommendation of preventive measures.

Development part of the project will try to provide novel analytical tools regarding to project topics and methods. The first, a standardized kit assay for the direct apply to routine laboratory testing in case of particular diseases. The second, a biosensor being based on high nanotechnology knowledge should provide chipper and more efficient instrument for DNA analysis worked out by genomic group and tested by them during the project period.