

# **Model of stress-induced cellular adaptation**

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### **Summary**

Adaptation is a fundamental process that occurs not only at the level of organisms, but also at the level of individual cells. This level of adaptation underlies the solution of many practical problems including mammalian life-style diseases, different types of cancer, antibiotic or pest resistant organisms and so on. Recent studies of tumorigenic transformations in mammals and adaptive mutagenesis in bacteria show striking similarity in biological processes imposed by sustained stress environment at the level of individual cells. They indicate that there are inherent fundamental mechanisms in each cell that epigenetically reprogram cellular genome in response to this environment. The reprogramming primes genome for the mutational modifications and directs mutations to genes that are under selection pressure in the environment. At present these mechanisms are not understood and even their existence is heatedly debated, because they violate the principal statement of Neo-Darwinism about the stochastic nature of mutations. The goal of this study is (i) to identify specific adaptation mechanisms in the model organisms implemented at the cellular level of their organization; (ii) to develop tailored gene databases of stress-induced cellular adaptation for the model organisms; (iii) to reveal common (between model organisms) biological processes, metabolic pathways, molecular functions and genes underlying the mechanism of cellular adaptation and generalize this information as the model of stress-induced cellular adaptation; (iv) to get experimental confirmation for the model.

An analytical consideration of the published literature on the model organisms, structural organization of the collected information, comparative genomic analysis of the model organisms, mathematical analysis of gene array experiments related to cellular adaptation (studies of cancer, senescence, stationary state mutagenesis, exposures of cell culture with toxins and so on), which are available in public repositories, will be employed to accomplish the objectives of the study.

A website will be developed to disseminate the collected information, the databases and the proposed model to scientific society.

The model of cellular adaptation has many important implications, because it provides insight into fundamental mechanisms operated at cellular level of organization. This insight will improve and extend our approaches (i) to diagnostics, prevention and treatment of cancer, (ii) to studies of senescence and embryonic development. Understanding of molecular mechanisms involved in stress-induced cellular adaptation will foster solution of many vital practical problems related to quick adaptation of microorganisms to the environment including antibiotic or pest resistant microorganisms. Revealing of crucial metabolic pathways and genes involved in cellular adaptation as well as environmental conditions for their activation will promote the development of new technologies for creating organisms with given beneficial traits. It seems to be especially promising for microbes and plants. The molecular mechanisms of cellular reprogramming identified in the model will provide insight into cellular mechanisms underlying embryonic development and facilitate solution of problems related to efficient nuclear cloning and stem cells differentiation. The model will contribute to the training of students in the biological sciences providing general principles of cellular response to different environmental conditions.

## Objectives

The main objectives of the proposed study are to validate the hypothesis by analytical consideration of genomic and biochemical studies on different model organisms, to expand the hypothesis into the Model of Stress-induced Cellular Adaptation and to confirm the model by gene array experiments related to cellular adaptation of the model organisms. It will be accomplished by the following consecutive steps (Figure 1):

(1) Collection of the scientific information on the model organisms to identify specific mechanisms of adaptation implemented at the cellular level of their organization.

(2) Development of the tailored Gene Databases of Stress-induced Cellular Adaptation (GDSCAs) for the model organisms and their population with the collected information to facilitate the analytical consideration and comparative analysis of the model organisms.

(3) Analytical consideration of the information collected in the databases accompanied by the comparative genomic analysis of the model organism to reveal common (between model organisms) biological processes, metabolic pathways, molecular functions and genes underlying the mechanism of cellular adaptation.

(4) Development of the Model of Stress-induced Cellular Adaptation (MSCA).

(5) Experimental confirmation of the MSCA by comprehensive mathematical analysis of gene array experiments related to cellular adaptation (studies of cancer, senescence, stationary state mutagenesis, exposures of cell culture with toxins and so on).

(6) Dissemination of the information collected in the databases and the MSCA to scientific society.

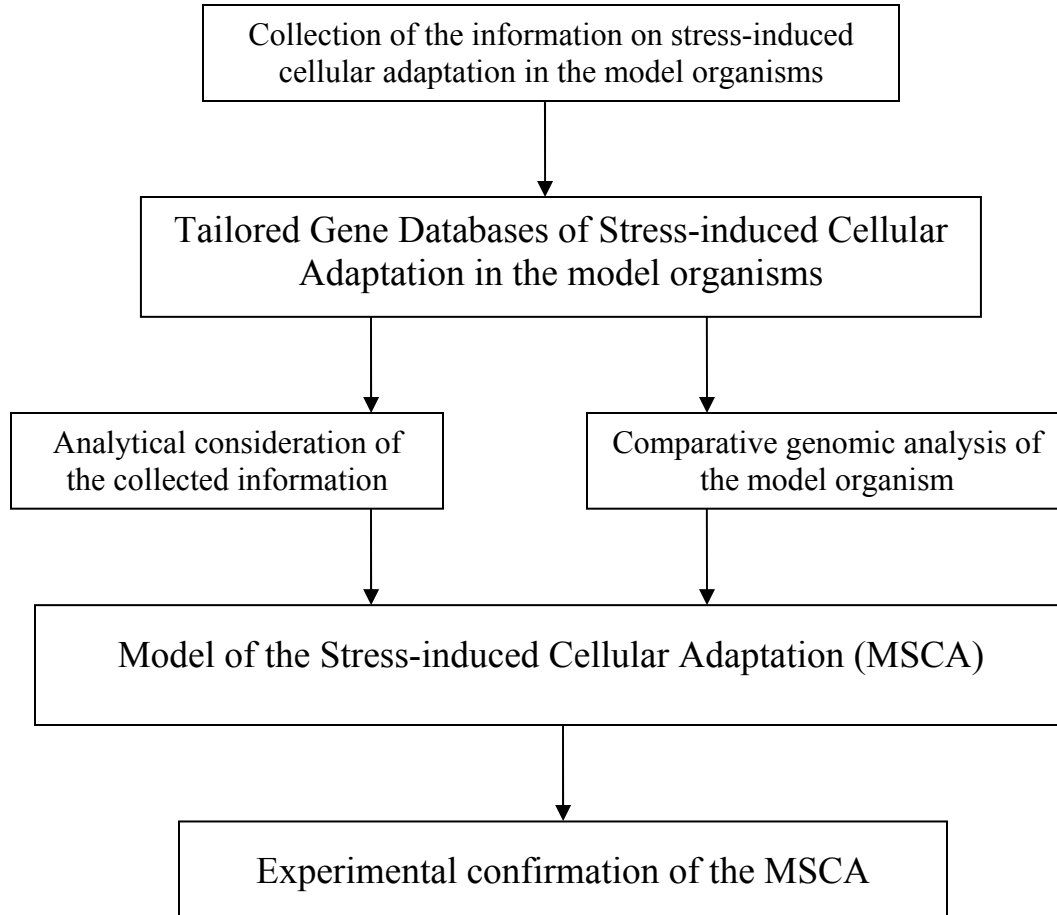


Fig.1. Objectives of the study