

**Scientific report for the project PN-II-ID-PCE-2011-3-0571, period april 2012 –  
december 2014, Stages I, II, III, cumulative**

**Activities of each stage:**

**Stage I**

1. Experiments to get more biological data to be used in mathematical modeling. New data on the apoptosis, proliferation and the transfer of thymocytes between main subpopulations, and the dynamics of medullary and stromal cells of the thymus.
2. Generation of a mathematical model of the first stages of thymus regeneration and the inverted CD4+ single-positive/CD8+ single-positive ratio in the regenerated thymus.

**Stage II**

1. Finishing the mathematical model of the first stages of thymus regeneration and the inverted CD4+ single-positive/CD8+ single-positive ratio in the regenerated thymus.

**Stage III**

1. Modeling the inverted CD4+single-positive/CD8+single-positive thymocyte ratio in the regenerated thymus.
2. Modeling the apoptosis of thymocytes in the involuting and regenerating thymus under the influence of glucocorticoids.

**Objectives:**

**Stage I** - to publish two ISI-indexed papers from these results with members of the project as principal authors;

**Stage II** – to publish one ISI-indexed, impact factor paper, from these results with members of the project as principal authors;

**Stage III** - to publish one ISI-indexed, impact factor paper, from these results with members of the project as principal authors;

**Results:**

**Stage I**

1. In this stage we submitted to publication a paper that we got eventually approved on the dynamics of

macrophages in the diabetic thymus. The main authors are members of the project.

**Accumulation of tissue macrophages and depletion of resident macrophages in the diabetic thymus in response to hyperglycemia-induced thymocyte apoptosis.**

Barbu-Tudoran L, Gavriliuc OI, Paunescu V, Mic FA.

Journal of Diabetes and its Complications. 2013 Mar-Apr;27(2):114-22.

2. We have completed and submitted to publication (at **Molecular Systems Biology**) another paper that deals with the mathematical modeling of glucocorticoid-induced thymus involution and regeneration. All authors are members of the project.

**Mathematical modeling with perturbation functions of the drug's mechanism of action on thymocyte populations during glucocorticoid-induced thymus involution and regeneration.**

Daniela Zaharie, Radu Dumitru Moleriu, Lavinia Cristina Moleriu, Ioan Nicolae Casu, Alexandra Teodora Gruia, Ani Aurora Mic Virgil Paunescu, Felix Aurel Mic.

3. We have presented a paper at SYNASC 2012, the 14th International Symposium on Symbolic and Numeric Algorithms for Scientific Computing, held at Universitatea de Vest Timisoara, Romania, between 26-29 september, 2012. All three authors are members of the project.

**- Stability analysis and its impact on the parameters estimation for a logistic growth model.**

Lavinia Moleriu, Radu Moleriu and Daniela Zaharie

4. We have presented a paper at "The 13<sup>th</sup> International Conference on Mathematics and its Applications ICMA2012", Politechnica University of Timisoara, Romania, section Probability and Statistics. Applications in Health and Clinical Research, held in Timisoara, november 1-3, 2012. The author is a member of the project.

**Inferring evolution models from experimental data on populations of thymocytes.**

Lavinia Cristina Moatar-Moleriu

**Stage II**

1. We published a paper in the conference volume of the Genetic and Evolutionary Computation Conference, Amsterdam, The Netherlands, July 6-10, 2013 (<http://www.sigevo.org/gecco-2013/>). The first two authors are members of the project. The paper is indexed in the main databases and is available at <http://dl.acm.org/citation.cfm?doi=2463372.2463408>

**Particularities of Evolutionary Parameter Estimation in Multi-stage Compartmental Models of**

## **Thymocyte Dynamics.**

Daniela Zaharie, Lavinia Moatar-Moleriu, Viorel Negru

2. We published a paper in the conference volume of the 9th International Conference on "Large-Scale Scientific Computations" June 3-7, 2013, Sozopol, Bulgaria. The first and the last authors are members of the project.

### **Evolutionary Estimation of Parameters in Computational Models of Thymocyte Dynamics.**

Lavinia Cristina Moatar-Moleriu, Viorel. Negru, Daniela Zaharie

## **Stage III**

1. We published a paper in the Journal of Theoretical Biology that shows a mathematical model of the involuting and regenerating thymus, which addresses the role of apoptosis in these events and explains the mechanism of the inverted ratio of CD4+single-positive/CD8+single-positive thymocytes in the regenerated thymus. All authors are members of the project.

### **Insights into the mechanisms of thymus involution and regeneration by modeling the glucocorticoid-induced perturbation of thymocyte populations dynamics.**

Moleriu RD, Zaharie D, Moatar-Moleriu LC, Gruia AT, Mic AA, Mic FA.

J Theor Biol. 2014 May 7;348:80-99.

2. We have resubmitted a revision of our manuscript to the journal Differentiation in which we document the involvement of trogocytosis in the interactions between mesenchymal stem cells from thymus and thymocytes in vivo. All main authors are members of the project.

### **Trogocytosis supports the viability and differentiation of thymocytes in autologous co- cultures with mesenchymal stromal cells .**

Seyed Mohammad Reza Azghadi, Maria Suciu, Alexandra Teodora Gruia, Lucian Barbu-Tudoran, Mirabela Iustina Cristea, Ani Aurora Mic, Virgil Paunescu, Danina Muntean, Felix Aurel Mic.

Differentiation, DIFF-D-14-00074R1

3. We have submitted a manuscript to Molecular and Cellular Endocrinology that is currently Under Review, that deals with the molecular mechanism of glucocorticoid's action on thymocyte homeostasis in the diabetic thymus. All main authors are members of the project.

### **Corticosterone perturbs the apoptotic gene machinery of thymocytes in the diabetic thymus**

**leading to persistent organ involution.**

Ani A. Mic, Alexandra T. Gruia, Maria Suci, Seyed Mohammad Reza Azghadi, Oana I. Gavriiuc, Valentin L. Ordodi, Virgil Paunescu, Felix A. Mic.  
Molecular and Cellular Endocrinology, MCE-D-14-00600

4. We have submitted a manuscript to Comparative Medicine that shows in mouse the detailed changes in the thymocyte subpopulations during thymus involution in diabetes and the mechanisms by which they occur. All main authors are members of the project.

**Diabetes impairs thymocyte proliferation and causes thymocyte apoptosis with subsequent thymus involution.**

Ani A. Mic, Oana I. Gavriiuc, Alexandra T. Gruia, Maria Suci, Valentin L. Ordodi, Virgil Paunescu, Felix A. Mic.  
Comparative Medicine - CM-14-000127

5. We have finished the experimentation and the Gompertzian modeling for another manuscript in which we model the apoptosis of thymocytes and the dynamics of thymocyte populations in the pre-natal and post-natal thymus in mice. We intend to submit the manuscript to Journal of Immunology and all authors on it are members of the project.

**Gompertzian modeling of thymocyte homeostasis in the murine thymus shows that post-natal thymus is independent of the inflow of bone marrow progenitors.**

Daniela Zaharie, Moleriu Radu Dumitru, Moleriu Lavinia Cristina, Felix Aurel Mic

6. We have presented two posters at the EMBO Workshop „Complex Systems in Immunology”, Singapore, december 2-4, 2013.

**- Insights into the mechanisms of thymus involution and regeneration by modeling the glucocorticoid-induced perturbation of thymocyte populations dynamics.**

Moleriu RD, Zaharie D, Moatar-Moleriu LC, Gruia AT, Mic AA, Mic FA.

**- Gompertzian modeling of thymus evolution reveals different dynamics of thymocyte generation in pre- and post-natal periods.**

Daniela Zaharie, Radu Dumitru Moleriu, Lavinia Cristina Moatar-Moleriu, Alexandra Teodora Gruia, Ani Aurora Mic, Felix Aurel Mic.

7. We have presented two posters at the Young Researchers in Biosciences (International Symposium)

Cluj Napoca, july 23-27, 2014.

**- Stromal macrophages dynamics in diabetic thymus.**

Alexandra Teodora Gruia, Lucian Barbu-Tudoran, Ani Aurora Mic, Valentin Laurentiu Ordodi, Oana Isabella Gavriiuc, Maria Suciu, Virgil Paunescu, Felix Aurel Mic.

**- Membrane Communication of MSCs and Thymocytes in Autologous Co-culture Generates Mature T-cells in vitro.**

Seyed Mohammad Reza Azghadi, Alexandra Teodora Gruia, Lucian Barbu-Tudoran, Ani Aurora Mic, Valentin Laurentiu Ordodi, Maria Suciu, Virgil Paunescu, Felix Aurel Mic.

8. We have presented an oral communication at the National Conference of the Romania Society of Cell Biology, Targu-Mures, Romania, june 4-7, 2014.

**Components of the inflammatory and stress reaction cause thymus involution in experimental diabetes.**

Suciu Maria, Alexandra Teodora Gruia, Seyed Muhammad Reza Azghadi, Oana Gavriiuc, Ani Aurora Mic, Valentin Ordodi, Virgil Paunescu, Felix Aurel Mic.



Project manager, Dr. Mic Aurel Felix