**PERSONALIZED GENOMICS LAB**

**What We Do**

We use Illumina NextSeq 550 and Agilent gene expression microarrays to profile the transcriptomes of cells and tissues from humans and animal models of human diseases. An original algorithm determines the Gene Master Regulators (GMR) of cancer nuclei in solid and liquid biopsies, or pathogens in blood and urine samples. Through various methods of gene editing we manipulate the GMR’s expression to selectively destroy the “bad” cells with minimal impact on the “good” ones. Owing to the unrepeatable set of contributing factors, each patient is unique and thus are his/her GMRs.

**Contact Us**

**Personalized Genomics Laboratory**

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TEAM

**About Us**

We perform a wide range of **experimental\*** and **theoretical\*\*** genomics studies aiming to identify and edit the genes responsible for cancer and drug resistance phenotypes.

\*open a window presenting the experimental methods and the lab equipment

1. **Preparatory techniques:**

- DNA, RNA and protein extraction, purification,   
- RNA reverse transcription and fluorescent labeling  
- DNA and proteins fluorescent labeling  
- DNA, RNA and protein concentration (NanoDrop)  
- DNA, RNA, proteins concentration and QC (Bioanalyzer)  
- Western blotting  
- SpeedVac concentration of proteins, DNAs and RNAs  
- Controlled PCR amplification  
  
**B. Hybridization of Agilent microarrays:**  
- Whole Genome Gene Expression microarrays for 30+ species   
- Exon microarrays (human, mouse, rat)   
- miRNA microarrays  
- CGH (Comparative Genomic Hybridization) microarrays  
- CGH+SNP (Single Nucleotide Polymorphism) microarrays  
- CNV (Copy Number Variant) microarrays  
- ChIP-on-chip (Chromatin ImmunoPrecipitation) microarrays  
- DNA methylation (CpG islands) microarrays

**C. Hybridization of Illumina beadchips:**  
- Whole Genome Expression BeadChips: human, mouse, rat   
- Infinium iSelect HD custom genotyping BeadChips for  
   virtually all species  
- Infinium HumanMethylation450 BeadChip  
- Infinium HumanCytoSNP-FFPE-12 BeadChips  
- Infinium Human Omni Express-FFPE BeadChips

**D. Hybridization and scanning of custom arrays:**  
- cDNA microarrays   
- oligonucleotide microarrays  
- protein/antibody arrays

\*\*open a window listing the analyses (algorithms, software and examples-paper in Biological Theory)

**A. Computational Genomics:**

- Noise analysis of various ‘omics’ platforms  
- Feature extraction, primary analysis, export in selective formats, organization of searchable dbases and deposit into NCBI and other public dbases  
- Normalization and filtration of ‘omics’ data   
- Determination of gene expression level, control, coordination and commanding height    
- Analysis of the Regulome

- Weighted Pathway Regulation Analysis  
- Prominent Gene Analysis   
- Pair-Wise Relevant Analysis  
- Transcriptomic Distance Analysis  
- Transcriptomic Recovery Analysis   
  
**B. Bioinformatics:**

- Agilent Feature Extraction, Axon GenePix + Acuity, Illumina Genome Studio  
- Gene ontology (GO) analysis  
- Pathway analysis (KEGG, Amigo, Ingenuity, GeneMap, DAVID)  
- Identification and quantification of significantly altered functional pathways   
- Determine composition, topology and interplay of functional genomic fabrics  
- Determine remodeling of functional genomic fabrics and their interplay during development/hormonal cycle/disease progression/treatment  
- Quantify the overall transcriptomic recovery in response to a therapy

**C. Biostatistics:**  
- Optimize information-to-cost experimental design, select study population, define outcomes and determine sample size and number of technical and biological replicas;  
- Perform various statistical tests on experimental data  
- Normalize, filter and perform statistical analysis of pathophysiological and ‘omic’ data;  
- Collect, perform primary analysis, export in selective formats, organize in searchable dbases and prepare data for deposit into public repositories;  
- Assistance with Origin Pro, GraphPad Office, Excel and Mathematica

**D. Computational Biology/Mathematical modeling:**  
- Develop (classical/quantum) physics and (continuous/discrete, deterministic/stochastic) mathematical models of complex biological systems/phenomena  
- Run numerical simulations of mathematical models  
- Determine the dynamics of the overall pathophysiological and transcriptomic changes during development, hormonal cycle, progression of a disease and recovery in response to a therapy.

**Assistance to write grant applications, reports and book chapters**.

**Our Team**

**Dumitru A Iacobaş, PhD, Principal Investigator\***

Research Professor and PGL Director

*Develops the concepts and mathematical algorithms*

*Design the experiments and perform the analyses of the experimental data*

**TBN Postdoctoral Researcher**

*Performs the transcriptomics and molecular biology experiments*

*Optimizes the experimental methods*

**Nneka Ede Graduate Student Researcher\***

*Assist the PI in the development of mathematical analyses*

*Develops the necessary software*

*Assist the PI with the analysis of the experimental data*

**TBN Graduate Student Researcher/Technician**

*Assist the Postdoctoral Researcher at genomics experiments*

*Maintains the equipment and the consumables*

\*open a window with the **layout** and **CV** of the team member

**Iacobas layout:**

I am an expert in both experimental and computational genomics. I was also involved in the technology development, performed analyses of the technical noise of microarray platforms and took care of transgenic mouse colonies and genetically engineered cell cultures. My lab has profiled a wide diversity of tissues and cell cultures from blood and various regions of brain, spinal cord, retina, heart, liver, kidney, lung, thyroid and prostate. Through collaboration with other groups, we have studied transcriptomic alterations in neurodegenerative, cardiovascular and infectious (with *Tripanosoma cruzi*, *Plasmodium berghei*, *Borrelia burgdorferi* and *Enteroccocus faecium*) diseases, and following hypoxic or low gravity stress. The tissues and cells were collected from humans but also from animal (mouse, rat, rabbit, dog, chicken embryo) models of human diseases. In our studies, we have used cDNA and oligonucleotide microarrays (printed by Agilent but also by Einstein, Yale, Rockefeller and Duke University Core Facilities), Affimetrix, Illumina beadchips and RNA sequencers (Illumina MySeq and NextSeq550). I have introduced the “multiple yellow” design (offering the best use of resources), optimized the experimental protocols and developed a powerful normalization algorithm that reduces the technical noise from 30% to 20%. I was the first to consider gene expression variability and expression coordination in addition to the average expression level in biological replicas that increased by an order of magnitude the information provided by transcriptomic studies. My main contribution to the theoretical genomics is the introduction of the Genomic Fabric Paradigm and the development of the mathematically advanced analyses of the Relative Expression Estimate, Coordination Power, Pair-Wise Relevance and Gene Master Regulators. My qualification and experience in all branches of the genomics research is quite unique, almost all investigators being qualified in only one (technological, functional, experimental, computational or bioinformatics) aspect. As such, I can fully conduct the research, train personnel and understand and overcome all problems that may occur during the proposed studies.

**Education:** PhD (Bio)Physics - University of Bucharest, Romania

**Research Funding:** $1,203,000 as P.I., $12,970,000 as Co-P.I., $19,322,000 as Investigator

**Publications:**

- 3 (Romanian) patents in microelectrophysiology and 10 innovations in genomics and nuclear medicine

- 7 books in a total of 22 editions (published in Romanian, some also in English, Spanish and Greek)

- 86 articles in peer-reviewed journals

- 27 chapters in peer-reviewed scientific books and conference proceedings

- 79 genomic experimental datasets, 7 bioprojects, 22 proteins, 5 nucleotides published in [www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)

**Current Projects**

**PVAMU ORISP USRF PI N Ede (advisor DA Iacobas)**

Development of Cancer GMR Software Package for Personalized Cancer Gene Therapy

*This Project develops all the computer software programs needed to efficiently do the calculations for determining the Gene Master Regulators (GMRs) on a large-scale level. All software programs are being designed using the Anaconda distribution of Python 3 with statistical and graphical user interface packages such as SciPy and Tkinter. The GMR Software Package will include executable programs to determine the functional pathways from the Kyoto Encyclopedia of Genes and Genomes (KEGG) Database, the Gene Commanding Height (GCH) and Weighted Pathway Regulation (WPR).*

**CPRIT-HIHR (submitted) PI DA Iacobas**

Gene Master Regulators Approach for Personalized Cancer Gene Therapy

*Studies proposed in this Application will test on blood, brain, lung, prostate and thyroid standard human cancer cell lines that silencing the Gene Master Regulators kills selectively the cells it commands.* **Specific Aims\***

\*open window:

***Specific Aim 1: To determine the Gene Commanding Height (GCH) hierarchy in standard prostate, lung, thyroid and blood human cancer cell lines.*** We will use Next Gen RNA sequencing (Illumina NextSeq 550) and/or (Agilent 4x44k human gene expression) microarray platform, both available at our PVAMU Computational Systems Biology Center – Personalized Genomics Laboratory to profile cancer cell lines purchased from authorized vendors. We will use our Genomic Fabric Paradigm as well as the standard experimental protocol and data processing algorithms established and validated in hundreds of genomic experiments performed in previous IacobasLabs from Albert Einstein College of Medicine and New York Medical College.

***Specific Aim 2: To reprogram cancer cell lines using CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) gene editing, lentiviral transfection or siRNA.*** We will design custom CRISPR clones of the selected GMRs, order them to a specialized company (<https://www.sigmaaldrich.com>, <http://www.crisprtx.com>, <https://www.editasmedicine.com/crispr>) and reprogram the cancer cell lines studied at SA1. As alternatives to CRISPR we can use lentiviral transfection or siRNA for which we have experience.

***Specific Aim 3: To evaluate the effect of CRISPR-GMR reprograming in the survival of the treated cancer cells.*** The viability of cancer cells (the growth rate and the death rate) will be assessed before and after the treatment.

**PVAMU ORISP FRDGP (submitted) PI DA Iacobas**

Complement C5ar1 Antagonists for the Treatment of Autism Spectrum Disorders

*This is part of a long standing research collaboration of Iacobaslab with the labs of Dr. Velisek (New York Medical College-NYMD), Dr. Veliskova (NYMC), Dr. Borges (Queensland University School of Biomedical Sciences) and Dr. Chachua (Danbury Hospital, CT). We use Dr. Velisek’s ASD rat model to test whether PMX53, a complement C5ar1 antagonist, is efficient in restoring the synaptic neurotransmission in the hypothalamic paraventricular node altered by NMDA-triggered the autism spectrum disorder (ASD). Dr. Chachua isolates the paraventricular nodes collected from male and female rats exposed to five experimental conditions. Our studies run in parallel with electrophysiological studies performed by the group of Dr. Velisekova, behavioral studies performed by the group of Dr. Velisek and physio-pathological studies performed by the group of Dr. Borges.*

**Specific Aims\***

\*open window:

Our working hypothesis is that *PMX53 treatment recovers the ASD-associated alterations of synaptic neurotransmission caused by the modulatory inflammatory pathways on brain circuitries*.

***Specific Aim 1: To determine the transcriptomic alterations of the synaptic neurotransmission in the hypothalamic paraventricular node of an ASD rat model.***

***Specific Aim 2: To determine the recovery of the synaptic transmission following treatment with the anti-inflammatory agent PMX53.***

**COLLABORATORS & COAUTHORS**

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**PUBLICATIONS**

6 **Iacobas DA,** Velisek L. (2018)Regeneration of neurotransmission transcriptome in a model of epileptic encephalopathy after antiinflammatory treatment. *Neural Regen Res*, 13(10):1715-1718, PMCID: PMC6128045, doi: 10.4103/1673-5374.238607, **IF = 2.234. Open access.** <https://www.ncbi.nlm.nih.gov/pubmed/30136682>

5 Kobets T, Iatropoulos MJ, Duan JD, Brunnemann KD, **Iacobas DA**, Iacobas S , Vock E, Deschl U, Williams GM: Effects of Nitrosamines on the Expression of Genes Involved in Xenobiotic Metabolism in the Chicken Egg Alternative Genotoxicity Model. *Toxicol Sci*, 166(1), 82–96, doi: 10.1093/toxsci/kfy197. PMID: 30102407. **IF = 4.181.** <https://www.ncbi.nlm.nih.gov/pubmed/30102407>

4 **Iacobas DA**, Iacobas S, Nebieridze N, Velisek L, Veliskova J (2018): Estrogen protects neurotransmission transcriptome during status epilepticus, *Front Neurosci*. 12:332. DOI: 10.3389/fnins.2018.00332. PMCID: PMC6019481. **IF =4.294.** **Open access.** <https://www.ncbi.nlm.nih.gov/pubmed/29973860>

3 **Iacobas DA**, Chachua T, Iacobas S, Benson MJ, Borges K, Veliskova J, Velisek L. (2018). ACTH and PMX53 recover the normal synaptic transcriptome in a rat model of infantile spasms. *Sci Rep.*8:5722, DOI:10.1038/s41598-018-24013-x.PMCID: PMC5893534. **IF = 5.312. Open access.** <https://www.ncbi.nlm.nih.gov/pubmed/29636502>

2 **Iacobas DA**, Tuli N, Iacobas S, Rasamny JK, Moscatello A, Geliebter J, Tiwari RM. (2018). Gene master regulators of papillary and anaplastic thyroid cancer phenotypes. *Oncotarget* 9(2), 2410-2424. doi: 10.18632/oncotarget.23417. PMCID: PMC5788649. **IF = 6.36. Open access.** <https://www.ncbi.nlm.nih.gov/pubmed/29416781>

1 **Iacobas DA**, Iacobas S, Tanowitz HB, deCarvalho AC, Spray DC (2018). Functional genomic fabrics are remodeled in a mouse model of Chagasic cardiomyopathy and restored following cell therapy. *Microbes Infect.* 20(3), 185-195. doi: 10.1016/j.micinf.2017.11.003. PMID: 29158000. **IF = 2.924.** <https://www.ncbi.nlm.nih.gov/pubmed/29158000>

**b. Submitted:**

2. **Iacobas DA,** Iacobas S, Lee PR, Cohen JE, Fields RD. Covariance analysis identifies coordinated activity of transcriptional networks responding to the pattern of action potential firing in neurons. *Sci Rep*

1. **Iacobas DA,** Ede N,Iacobas S. The GMR approach of cancer gene therapy. *Physical Biol.*

**GENOMIC EXPERIMENTS**

7 **Iacobas DA,** Chachua T, Iacobas S, Benson M, Borges K, Veliskova J, Velisek L. (2018) Sex differences in the synaptic genomic fabrics of the rat hypothalamic paraventricular node [*Rattus norvegicus*] <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?&acc=GSE123721>

6 **Iacobas DA**, Iacobas S, K van Roosbroeck, Calin GA: Overexpression of miR-155 alters the hierarchy of gene master regulators in the adenocarcinomic human alveolar basal epithelial cell line A549 [*Homo sapiens*] <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE116575>

5 **Iacobas DA**, Iacobas S, K van Roosbroeck, Calin GA: Hierarchal gene master regulators of adenocarcinomic human alveolar basal epithelial cells A549 [*Homo sapiens*]

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE116361>

4 Kobets T, Iatropoulos MJ, Duan JD, Brunnemann KD, **Iacobas DA**, Iacobas S, Vock E, Deschl U, Williams GM: Genotoxicity of nitrosamines [*Gallus gallus*] <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE110906>

3 Kobets T, Iatropoulos MJ, Duan JD, Brunnemann KD, **Iacobas DA**, Iacobas S, Vock E, Deschl

U, Williams GM: Gene expression in chicken embryo liver [*Gallus gallus*] <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE110904>

2 **Iacobas DA**, Iacobas S: Proximity of oligodendrocytes remodels astrocytes' transcriptome [*Mus musculus*] <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE109035>

1 **Iacobas DA,** Iacobas S, Nebieridze N, Velisek L, Veliskova J: Estrogen protects neurotransmission transcriptome during status epilepticus [*Rattus norvegicus*] <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE107725>

**INTERNALTIONAL CONFERENCES**

5 **Iacobas DA:** “The Gene Master Regulators Approach Provides the Best Targets for the Personalized Cancer Gene Therapy”, International Conference on Disease Biomarkers and Precision Medicine (DBPM-2018), 10/22-24/2018 in Houston, TX. <https://unitedscientificgroup.com/conferences/disease-biomarkers-and-precision-medicine>

4 **Iacobas DA:** “Gene Master Regulators not Biomarkers should be tested for personalized cancer medicine”, 4th World Congress on Cancer Research & Therapy, Rome (**Italy**), 08/13-15/2018.

3 **Iacobas DA:** “Gene Master Regulators and the Personalized Timely Cancer Gene Therapy”, 3rd Intl. Conf on “Cancer Research and Targeted Therapy”, London, **UK**, 08/06-08/2018.

2 **Iacobas DA:** “The GMR Approach of Cancer Gene Therapy”, <http://q-bio.org/wp/qbconference>. Houston, TX, 06/26-29/2018

1 **Iacobas DA:** "Gene Master Regulators in Cancer Gene Therapy", 2nd Symposium of Translational Oncology STOP Cancer, Bucharest, **Romania**, 04/13-15/2018. **Videoconference:** <http://www.stop-cancer-romania.ro/en/prezentari/prezentari-2018/>

**SEMINARS**

5 **Iacobas DA:** “Gene Master Regulators approach may provide the most legitimate targets for cancer gene therapy”, **Baylor College of Medicine**, Houston 10/25/2018, host: Dr. Terzah, Division of Pediatric Hematology-Oncology.

4 **Iacobas DA:** “A physicist eye view on biology”, with the Graduate seminar of Dr. M Sadiku, PVAMU ECE, Prairie View, 10/9/2018. Host: Dr. M Sadiku

3 **Iacobas DA:** “A 3D pseudostochastic model of intercellular calcium signaling alteration in the diabetic smooth muscle”, Dept of Mathematics, College of Arts and Sciences, Prairie View A&M University, Prairie View 09/07/2018. Host Dr. N Hritonenko

2 **Iacobas DA:** “Alteration of calcium waves in the diabetic smooth muscle”, PVAMU – ECE, Prairie

View, 2/23/2018. Host: Dr. P Obiomon - Chair

1 **Iacobas DA:** “The personalized GMR approach of thyroid cancer gene therapy”, **MD Anderson Cancer Center**, Houston, TX, 1/26/2018. Host: Dr. G. Calin, Felix L. Haas Endowed Professor, Department of Experimental Therapeutics, Division of Cancer Medicine, Co-Director, The RNA Interference and non-coding RNA Center.