Reconstruction of a genome-scale metabolic model for chicken whole embryo considering transcriptomics data

Akberdin I.R.[1,2]*, Kulyashov M.A.[1,2], Volyanskaya A.R.[1], Kolmykov S.K.[1], Pintus S.S.[1], Yevshin I.S.[1], Guojun Sheng[3], Deviatiiarov R.M.[4], Stupina A.A.[4], Gusev O.A.[4,5], Kolpakov F.A.[1,2]

[1]*Sirius University of Science and Technology, Sochi, Russia*

[2]*Novosibirsk State University, Novosibirsk, Russia*

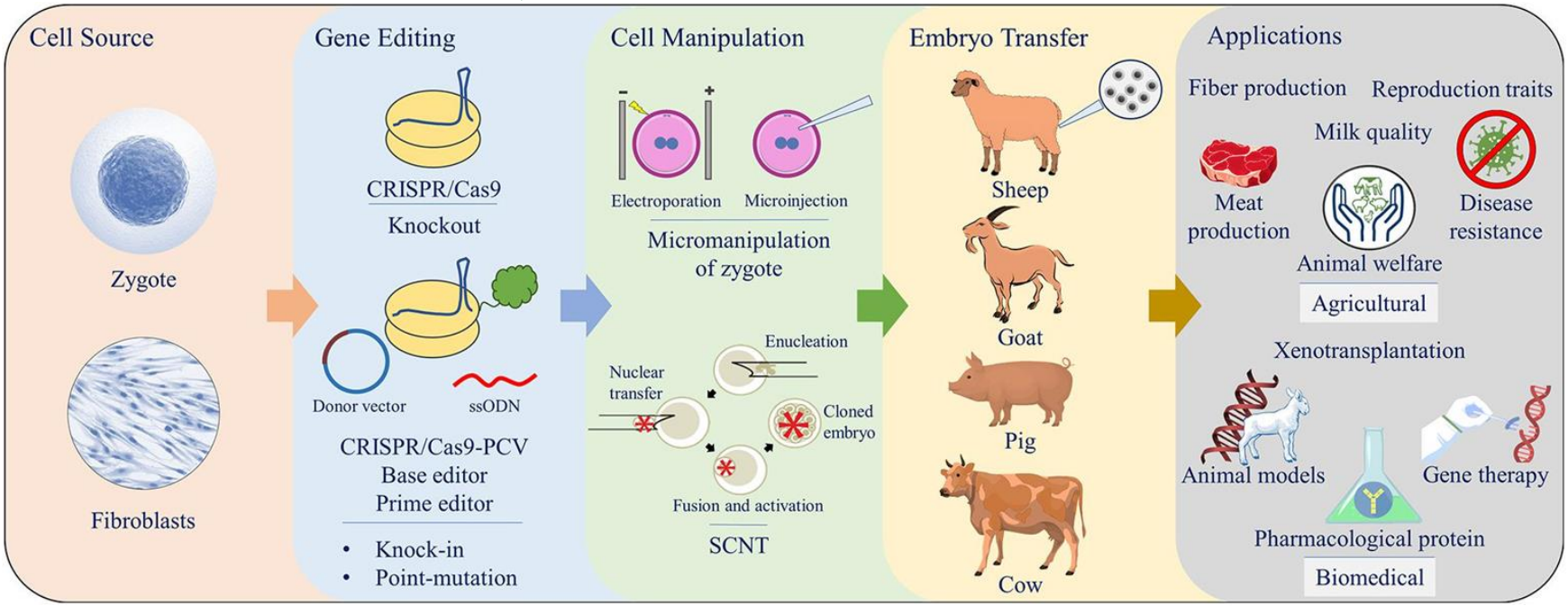
[3]*Kumamoto University, Kumamoto, Japan*

[4]*Regulatory Genomics Research Center, Kazan Federal University, Kazan, Russia*

[5]*Juntendo University, Tokyo, Japan*

* akberdinir@biosoft.ru

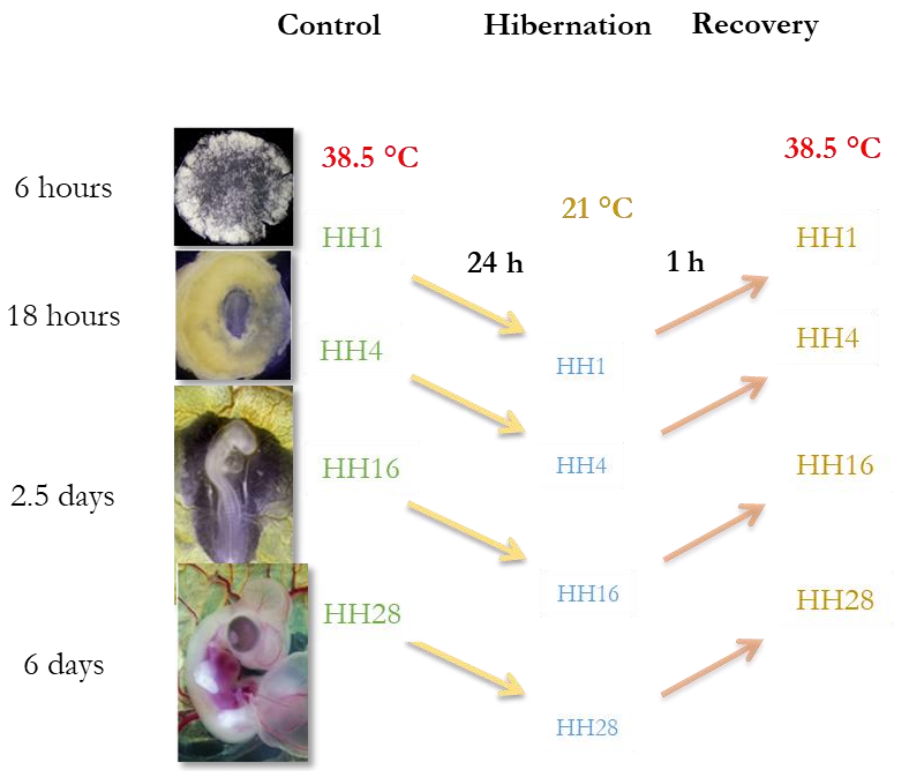
Research Objective: GET in investigations of livestock



Perisse *et al.,* 2021

Genetic modifications of model lab animals are mainly focused on basic research, while the application of **genetic engineering technologies (GET)** in investigations of **livestock** including **chicken** plays a key role in the capability to significantly extend existed or create a new niche market. However, a lack of both efficient approaches in the identification of **target genes, their regulatory elements determining desired traits and powerful mathematical models** enabling quantitative predictions of GE modifications hinders the implementation of this approach in livestock breeding.

Methods: Hibernation experiment and CAGE seq

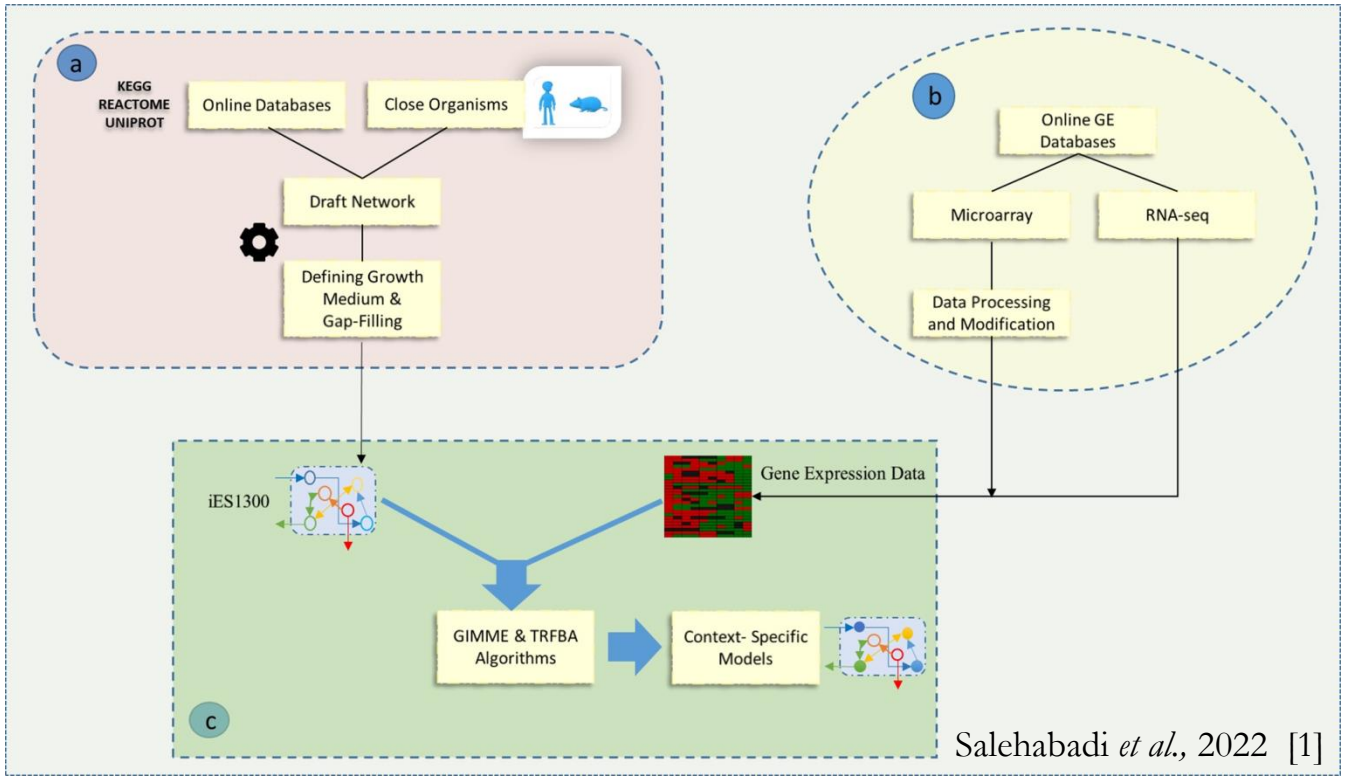


Total RNA was extracted from **36 embryos in total**. Single-read sequences were analyzed for quality and overrepresented adapter sequences with the theFastQC tool. Quality filtering and adapter trimming were performed with the Trimmomatic tool v0.39. Read mapping on the chicken genome GRCg6a was performed with the STAR local alignment tool. Statistical significance of differential expression of genes was calculated using the **DESeq2** and **edgeR** tools.

Deviatiiarov *et al.*, unpublished

A cap-analysis of gene expression (CAGE) of the chicken embryo in a goal to identify key pathways and networks responsible for hibernation ("cold torpor") adaptation in the amniote egg.

Methods: Reconstruction of a generic GSM network for chicken



Salehabadi *et al.*, 2022 [1]

Schematic representation of original model [1]:

(a) step-by-step genome-scale metabolic reconstruction and

(b) using transcriptomics data extracted by online gene expression databases

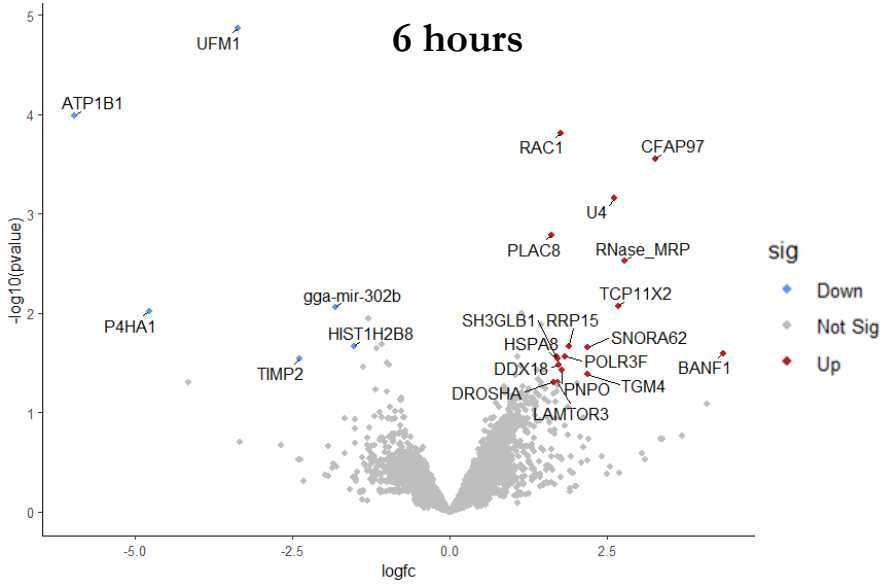
(c) to achieve context-specific models by the integration algorithms.

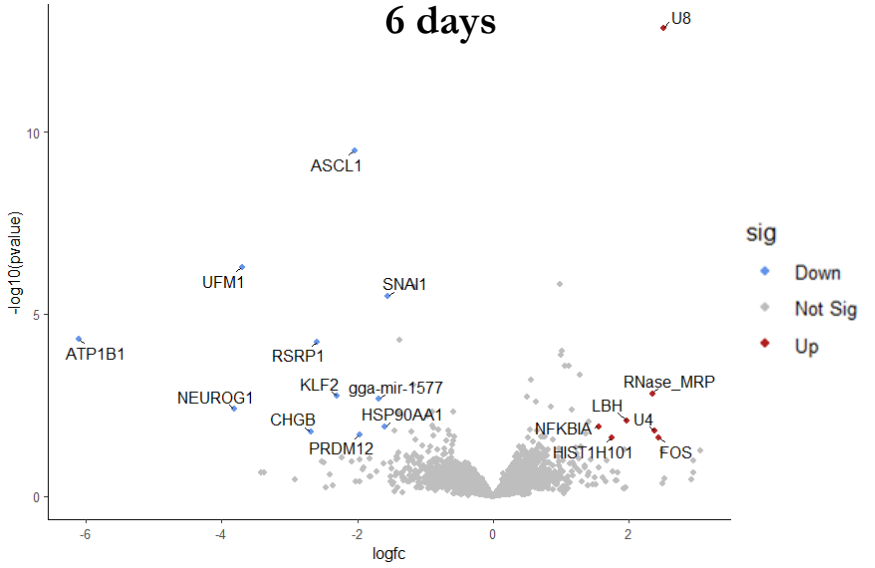
We utilized the recently published generic **genome-scale metabolic (GSM) model for chicken** [1]. Then we fine-tuned the model for chicken whole embryo knowledge and data based on the original transcriptomics data and **RIPTiDe** tool (Jenior *et al.*, 2020) in **BioUML** platform (Kolpakov *et al.*, 2021, *NAR*).

Results: Transcriptomics data analysis

Volcano plots of the differentially expressed genes using **DESeq2** for **control VS torpor** (6 hours VS 6 days)

p-value < 0.05 & (logFC < -1.5 & logFC > 1.5)





Term	RT	Genes	Count	%	P-Value
RNA processing	RT		5	22,7	1,1E-2
ncRNA metabolic process	RT		4	18,2	1,2E-2
rRNA processing	RT		3	13,6	1,8E-2
maturation of LSU-rRNA	RT		2	9,1	3,5E-2
ribosomal large subunit biogenesis	RT		2	9,1	8,4E-2

Term	RT	Genes	Count	%	P-Value
regulation of transcription from RNA polymerase II promoter	RT		4	23,5	5,2E-2
neuron differentiation	RT		2	11,8	8,7E-2
positive regulation of transcription from RNA polymerase II promoter	RT		3	17,6	9,0E-2
protein stabilization	RT		2	11,8	1,0E-1

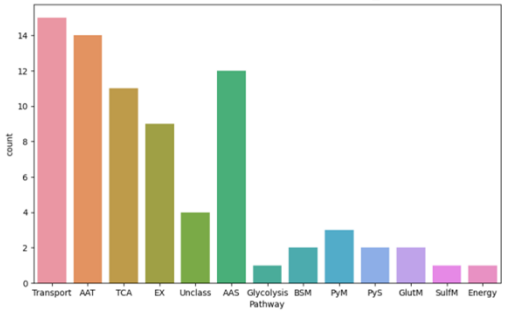
Conclusion: The analysis has demonstrated that genes that are differentially expressed (DEGs) due to the hibernation ("cold torpor") at the early stage of the embryo development (6 hours) are enriched in the biological processes related to RNA processing and metabolism, while DEGs at the late stage (6 days) are ontologically associated with transcription, differentiation processes as well as with the protein stabilization.

Results: parsimonious flux balance analysis(*pFBA*)

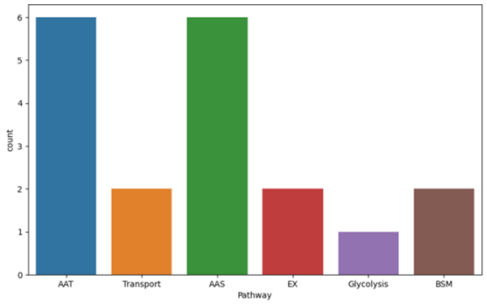
Metabolic pathways in which the flux changes are the most significant (control VS torpor)

A gene-encoded enzyme that catalyzes a reaction the flux value of which is significantly changed (control VS torpor)

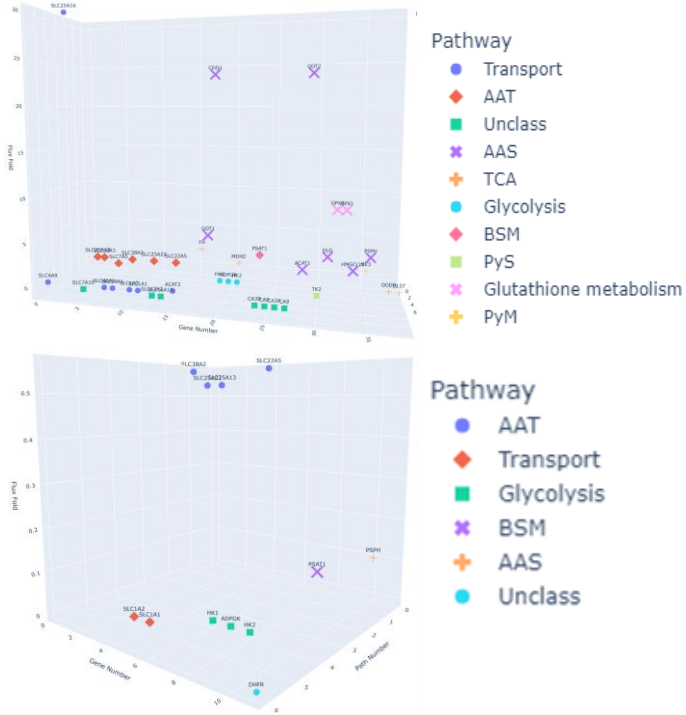
6 hours



6 days



AAS and AAT – amino acids synthesis and transport, respectively;
TCA – tricarboxylic acid cycle;
EX – exchange reactions;
PyM and PyS – pyruvate metabolism and pyrimidine synthesis, respectively; BSM - biosynthesis of secondary metabolites;



Conclusion: The transcriptome-guided pFBA of the genome-scale metabolic model for chicken has enabled the identification of the key metabolic pathways and demonstrated significant differences in the metabolic adaptation due to hypometabolic cold torpor between the early and late stages of the development.

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