10-12 November 2022

Szeged

XIX MEETING OF NOBEL LAUREATES AND TALENTED STUDENTS

The program of the National Biomedical Foundation

NEMZETI TUDÓSKÉPZŐ AKADÉMIA
NATIONAL ACADEMY OF SCIENTIST EDUCATION

VENUES

ACCOMMODATION

1. **Novotel Szeged** *(6721 Szeged, Maros u. 1.)*
2. **Tisza Hotel Szeged** *(6720 Szeged, Széchenyi tér 3.)*
3. **Szent János Hotel** *(6722 Szeged, Gutenberg u. 12.)*
4. **Art Hotel Szeged** *(6720 Szeged, Somogyi u. 16.)*
5. **Dóm Hotel** *(6720 Szeged, Bajza u. 6.)*

LECTURES, ROUND TABLE DISCUSSIONS, GALA EVENT, GALA DINNER

6. **József Attila Department of Education and Information Centre**
   (6722 Szeged, Ady tér 10.)

PRESS CONFERENCE

7. **City Hall Szeged**
   (6720 Szeged, Széchenyi tér 10.)

LABORATORY VISITS

8. **University of Szeged, Albert Szent-Györgyi Medical School**
   (Northern hospital garden)
9. **Biological Research Centre, Szeged** *(6726 Szeged, Temesvári krt. 62.)*

PROGRAM

10 NOVEMBER 2022 Thursday

17.00–20.00 ARRIVAL TO THE HOTELS, REGISTRATION

18.00–21.00 DINNER FOR HOTEL GUESTS

11 NOVEMBER 2022 Friday

07.00–08.30 BREAKFAST
In the hotels

08.00–08.45 ARRIVAL TO THE JÓZSEF ATTILA DEPARTMENT OF EDUCATION AND INFORMATION CENTRE, REGISTRATION

09.00–10.10 KEYNOTE PRESENATION
Congress hall
Chairmen: András Varró, Péter Hegyi

09.00–09.10 **Péter Hegyi:** *Laudation of Botond Roska*

09.10–09.50 **Botond Roska:** *Elements of Scientific Discovery*

09.50–10.10 **Discussion**

10.10–11.00 COFFEE BREAK
1st floor foyer and ground floor exhibition area

Parallel Program:

10.10–10.45 **Closed discussion of Botond Roska with the Szent-Györgyi Students**
Grand Hall

11.00–12.00 PRESENTATION OF THE SZENT-GYÖRGYI STUDENTS I.
Congress Hall
Chairmen: Zsuzsanna Helyes, Tamás Martinek

11.00–11.10 **Ákos Harangozó:** *Transcriptome analysis of Varicella Zoster virus using a multiplatform approach*

11.15–11.25 **Lili Kotmayer:** *Molecular oncohematology – the genetic background and modern treatment of leukaemias*

11.30–11.40 **Ákos Kovács:** *PCR for the detection of mutations A universal tool for nucleic acid based diagnosis*

11.45–11.55 **Miklós Lovas:** *Ascorbic acid derivatives*

Parallel Program:

11.00–12.00 **Round table discussions I.**
(upon preliminary assignment)
Szent-Györgyi Pupils meet the Szent-Györgyi Students
Basement, Auditorium I-II.

12.15–13.15 PRESENTATION OF THE SZENT-GYÖRGYI STUDENTS II.
Congress Hall
Chairmen: Mária Deli, Attila Mócsai

12.15–12.25 **Réka Sebestény:** *Creating a false fear memory with hippocampal interneurons*

12.30–12.40 **Benedek Szathmári:** *Yeast evolution and fungal quorum sensing*

12.45–12.55 **Enikő Tari:** *The effect of PACAP fragment in glaucomatous rat model*

13.00–13.10 **Simon Tusnády:** *The role of PLCγ2 in monosodium urate crystal-induced inflammatory processes*

Parallel Program:

12.15–13.15 **Round table discussions II.**
(upon preliminary assignment)
Szent-Györgyi Pupils meet the Szent-Györgyi Students
Basement, Auditorium I-II.

13.00–13.30 **Press Conference** (upon preliminary invitation)
City Hall Szeged, Lechner Lajos room

13.15–14.45 LUNCH
Hall

Parallel Program:

13.15–14.45 **Closed lunch of the Szent-Györgyi Mentors**
Ground floor exhibition area

15.30–16.50 PRESENTATION OF SZENT-GYÖRGYI MENTORS
Congress Hall
Chairmen: László Dux, Zoltán Papp

15.30–15.45 **Máté Manczinger:** *When less is more in antitumor immunity*

15.50–16.05 **László Virág:** *Role of DNA damage response proteins in cancer, inflammation and beyond*

16.10–16.25 **István Hernádi:** *Behavioural pharmacological „topmodels" in translational neuroscience: opportunities and challenges*

16.30–16.45 **László Acsády:** *Neuronal basis of stress induced behavioral alterations*

Each presentation is followed by a short discussion.

16.50–17.30 COFFEE BREAK
1st floor foyer and ground floor exhibition area

Parallel Program:

16.50–17.30 **Closed meeting of the Szent-Györgyi Students**
Grand Hall

17.30–18.40 PLENARY SESSION
Congress Hall
Chairmen: András Varró, Péter Hegyi

17.30–17.50 **Péter Hegyi:** *Introduction of the National Academy of Scientist Education*

17.50–18.10 **Presentation of certificates to Szent-Györgyi Senior teachers**

18.10–18.25 **Zoltán Rakonczay:** *The University Education Program of the National Academy of Scientist Education*

18.25–18.40 **'Szent-Györgyi Student of Excellence 2022' award ceremony, presentation of the awardee**
Anna Georgina Kopasz: *A versatile transposon-based technology for the validation of potential cancer „driver" alterations in the mouse liver*

18.40–18.50 PHOTO SHOOTING (upon preliminary assignment)
Congress hall

19.00–20.00 GALA EVENT
Hall

20.00–22.00 GALA DINNER
Hall

12 NOVEMBER 2022 Saturday

08.00–09.30 BREAKFAST
In the hotels

10.00–12.30 SZENT-GYÖRGYI PUPILS VISIT THE LABORATORIES OF THE SZENT-GYÖRGYI MENTORS
(upon preliminary assignment)

12.00–14.00 LUNCH, DEPARTURE

LECTURE ABSTRACTS

In the sequence of performance

ÁKOS HARANGOZÓ

Transcriptome analysis of Varicella Zoster virus using a multiplatform approach

Introduction: Varicella Zoster Virus (VZV) is a human pathogenic virus belonging to the subfamily Alphaherpesvirinae. It causes chickenpox in primary infection and shingles in reactivation from latency. The aim of our research was to generate the most accurately annotated transcriptome of Varicella Zoster virus.

Methods: Briefly, our own experiments consisted of cell culture, infection, RNA isolation, selection, quantitative and qualitative analysis, sequencing with MinION and bioinformatic analysis. In addition to our own data, we collected the available VZV transcriptomic data from the NCBI GenBank, which represents all uploaded sequencing raw files. In total, we used more than 2.5 billion reads from data from seven different research groups. In our bioinformatic analysis, sequenced reads were aligned to the VZV reference genome and then transcriptional start (TSS) and end (TES) positions as well as intron donor/acceptor positions were determined using different programs.

Results: 59 new splice isoforms and splice sites were detected. An important finding is that the long isoform of the ORF63 transcript contains several previously unknown splice variants near the replication origin. We have also discovered novel short and long transcript isoforms, embedded small ORFs, gene clusters producing tandemly oriented co-terminal transcripts, transcripts containing multiple splice variants, and complex transcripts up to 10 kbp in length.

LILI KOTMAYER

Molecular oncohematology – the genetic background and modern treatment of leukaemias

Oncohematology, the field of blood cancers, leukaemias and lymphomas, is one of the most prominent areas of cancer research, thanks to the wide range of molecular tests available and the dynamic development over the last decade. Easy availability of test materials, such as blood, bone marrow and lymphoid tissue samples, and the lower number of genetic variations compared to solid tumours, contribute to a rapid and precise understanding of the genetic background of haematological malignancies and facilitate the selection of the most effective treatment, which is of paramount importance in the era of personalised therapies.

Genetic changes of direct clinical relevance identified in hematological malignancies influence diagnostic and therapeutic decisions at several points in clinical practice. A small proportion of genetic abnormalities are specific to the disease and their

presence in combination with clinical signs is sufficient to establish the diagnosis. The Philadelphia chromosome, associated with chronic myeloid leukaemia (CML), was the first such genetic change to be identified, and the detection of the BCR-ABL1 fusion gene, which results from the translocation, has now become a prerequisite for the diagnosis of CML.

The development of the small molecule tyrosine kinase inhibitor imatinib to inhibit the BCR-ABL1 fusion gene was the first drug target and its specific inhibitor, the introduction of which has greatly improved the treatment of previously difficult-to-treat CML patients and has since been followed by the identification of many additional targets and the development of several inhibitors. These drugs significantly improve the life expectancy and quality of life of patients compared to conventional chemotherapy regimens, and therefore the identification of the mutation-bearing patient population benefiting most from personalised treatments by molecular testing is one of the most important tasks of modern oncohematological diagnostics.

In addition to establishing the diagnosis, specific abnormalities can also be used to monitor the disease, the so-called minimal or measurable residual disease (MRD), as the amount of these genetic abnormalities that can be measured in the test sample correlates with the number of tumour cells carrying the abnormality. In my presentation, I will not only describe molecular methods in the field of oncohematology, but also provide an insight into their potential applications and the molecular basis of modern personalised therapies.

ÁKOS KOVÁCS

PCR for the detection of mutations
A universal tool for nucleic acid based diagnosis

In the last years “PCR” became a hot topic, not only in science, but in everyday conversations. Most people however still don’t know what this Nobel-prize winning invention is. If you google it you would find that it’s an abbreviation stands for Polymerase Chain Reaction, and it is one of the most important tools of molecular biology. It was invented in 1983, by Kary Mullis and quickly revolutionized biochemistry, molecular biology, genetics, forensics and medicine. How does it work? How is it connected to the COVID-19 pandemic? I will explain it briefly. PCR is for the amplification of a specific part of the genetic material without any living cells, in a test tube using only enzymes and reagents with precisely set temperature cycles. Since every organism has unique genetic material, you can use it to detect or identify any organisms. Using in combination with other “magics” of biochemistry, you can identify even a person by PCR for example for paternity tests. For our research group another application is the most important. With the help of PCR, mutations can be identified. Mutations are the engines of evolution, however they can also cause diseases, such as cancer. By finding the carcinogenic mutation, treatment could be much more successful. Our research group has combined a set of tricks, and developed a new PCR based method for mutation detection to help the diagnosis and prognosis of cancer patients.

MIKLÓS LOVAS

Ascorbic acid derivatives

Ascorbic acid has long been known as a water-soluble vitamin and antioxidant. It participates in several biochemical processes (e.g. as a coenzyme in the synthesis of collagen). It is a relatively simple molecule, it can be described as a carbohydrate with an ene-diol structure; this special structure is what gives ascorbic acid its antioxidant property and also makes it acid. Despite this simple structure, not many derivatives of ascorbic acid have been synthesized compared to other carbohydrates. This is due to its chemical characteristics: it is prone to oxidation and subsequent degradation (especially at higher pH); and due to its acidic properties and highly polar nature, its derivatives are generally difficult to purify using conventional methods, making it a problematic compound to work with.

In our research we set out to prepare novel derivatives of ascorbic acid. We are currently working on conjugating a sulfur-containing analog of ascorbic acid with different biomolecules using UV-inititated thiol-ene addition in order to create hybrid molecules. The purpose of this glycosylation-analog modification is increasing the water solubility of the parent molecule, as well as endowing them antioxidant properties.

In my presentation I will be presenting a brief history of ascorbic acid, its special properties, the derivatives we have prepared, and the methodologies necessary for organic synthesis.

RÉKA SEBESTÉNY

Creating a false fear memory with hippocampal interneurons

Introduction: Neuronal assemblies in the hippocampus (HIPP) are large populations of neurons that are created by their own coordinated activity patterns. They have the ability store different contextual memories. Fear memories are associated to the context coding assembly that is the most active during a fearful event. Understanding how previous memories and neuronal activities influence the selection of these assemblies is essential for understanding the creation of true and false fear memories. Our recent findings revealed that the activity pattern of HIPP somatostatin (SOM) positive interneurons or their brainstem inputs could control HIPP memory acquisition and recall.

Aims: Here, we investigated the long-term plasticity of neuronal assemblies. We tested whether pre-activation of a neuronal assembly a day before a fearful contextual event can prepare it to store another fearful contextual event a day later with higher probability. We also hypothesized that the activity pattern of HIPP SOM interneurons is crucial in these associations.

Methods: We used optogenetic behavioral experiments, viral track tracing studies and neuroanatomical methods in transgenic animals that allowed us to investigate these questions in a brain region and cell type specific manner.

Results: Using optogenetic inhibition of a subpopulation of HIPP SOM interneurons (either directly or indirectly by activating their brainstem inhibitory inputs), we selectively activated a HIPP neuronal assembly. We then found that this assembly had preferentially encoded a fear memory a day later. We observed that mice showed fear memory even in an environment where they have never experienced fear in a context specific manner before.

Conclusion: Our preliminary findings suggest that manipulation of HIPP interneurons or their brainstem inputs can induce false associations. Understanding this kind of mechanism would be important in finding treatment in many types of anxiety-related mental conditions.

BENEDEK SZATHMÁRI

Yeast evolution and fungal quorum sensing

Understanding yeasts is of great importance for humanity. Besides industrially relevant species and model organisms among them, there are pathogenic yeasts that cause the death of millions per year. Their relevance notwithstanding, we know unworthily little about their evolution. What we know is that they are secondarily simplified, and the relationship between the independently emerged yeast groups can be characterized by the concept of latent homology.

Our aim is to broaden our knowledge on yeast evolution. We hypothesize that budding yeasts included in phylum Ascomycota derived from conidia (asexual propagules of filamentous fungi) that were constantly exposed to stress. We aim to create a mould species with yeast morphology using molecular methods to model the hypothesized evolutionary transition.

My subproject is built upon the assumption that if yeasts and conidia are homologous cells, then the latter might also demonstrate density-dependent behaviour, also known as quorum sensing (QS). This mechanism aims to synchronize population-wide metabolism by the secretion of signalling molecules into the medium. With a so called supernatant transfer experiment coupled with organic extraction I managed to demonstrate the presence of a QS-molecule in the medium of Aspergillus niger conidia. At present we are about to indentify this molecule. We are looking for one that is characteristic of conidia and yeasts, but not of hyphae.

I hope that my research will contribute to the creation of a gap-filler evolutionary concept regarding yeasts.

ENIKŐ TARI

The effect of PACAP fragment in glaucomatous rat model

Introduction: Glaucoma is one of the leading causes of blindness worldwide. A major risk factor of glaucoma is elevated intraocular pressure (IOP). PACAP acts through three receptors, of which PAC1 receptor has been shown to play the most important role in protection. A selective, PAC1-specific PACAP fragment may provide a potential therapeutic option in glaucoma.

Materials and Methods: Throughout the control examination, we examined the retinal morphology with optical coherence tomography (OCT) and functionality with electroretinography (ERG). We induced the elevated IOP by injecting microbeads (10µl) into the anterior chamber. In the control groups, the same amount of PBS buffer was used. Animals received either Systane or PACAP fragment (1mg/drop) containing eye drops for four weeks. The IOP was monitored for eight weeks. After eight weeks the OCT and ERG examinations were repeated.

Results: Microbeads injection significantly increased the IOP in the vehicle-treated glaucomatous group, however, PACAP fragment treatment indicated a decrease in the IOP. OCT scans showed a significant reduction in the total retinal thickness and in several different layers of the retina in the glaucomatous vehicle-treated group. In the same group, ERG a-wave was also significantly reduced. In the PACAP fragment-treated glaucomatous group both ERG and OCT images were similar compared to the control ones.

Conclusion: Our results show that PACAP fragment eye drop treatment exerted an IOP-reducing and neuroprotective effect.

SIMON TUSNÁDY

The role of PLCγ2 in monosodium urate crystal-induced inflammatory processes

Gouty arthritis characterized by recurrent severe inflammatory attacks of the joints, caused by monosodium urate (MSU) cyrstals deposition. The role of the neutrophils and macrophages in the pathogenesis of the MSU crystal-induced inflammation is well-known, however, the molecular pathomechanism is not fully understood.

In recent years, our research group has investigated the role of tyrosine kinase signaling pathways in autoantibody-induced inflammatory processes and has identified a number of essential signaling molecules. However, the role of the tyrosine kinase pathways and their important signaling component, phospholipase Cγ2 (PLCγ2), has not been clarified in the pathogenesis of gout. Therefore, our aim was to investigate the role of PLCγ2 in MSU crystal-induced neutrophil activation.

In our studies, the PLCγ2-deficient neutrophils showed dramatically impaired MSU crystal-induced ROS production, cytokine and chemokine release and MAP kinase activation compared to wild type cells, but lack of PLCγ2 did not affect the DNA externalization of the neutrophils in the presence of the crystals. Based on our results, PLCγ2 is an essential player in MSU crystal-induced neutrophil activation.

MÁTÉ MANCZINGER

When less is more in antitumor immunity

The immune system has a fundamental role in destroying tumor cells. Mutated cancer peptides are bound and presented by HLA molecules on the cell surface, which can induce an immune response. One would think that the presentation of more mutated peptides by these molecules makes it easier for the immune system to recognize cancer. However, this is not always the case. In my talk, I will present two examples. First, we showed that while certain variants of HLA molecules can present a much higher number of mutated peptides, they are associated with insufficient antitumor immunity and, thus, worse patient survival. The explanation for this is that the immune system is unable to differentiate mutated peptides from normal ones when they are presented in a high number by HLA molecules. Second, we found that the overly active presentation of cancer-associated mutations by HLA molecules during the early phase of cancer evolution selects for cancer cells that can effectively evade immune recognition. Immune evasion in these cells is often irreversible and associated with poor patient survival in late tumor stages. In sum, both examples indicate a golden mean in the immune recognition of cancer cells with potential implications for tumor immunotherapy.

LÁSZLÓ VIRÁG

Role of DNA damage response proteins in cancer, inflammation and beyond

An imbalance between the production and elimination of reactive oxygen species (ROS), known as oxidative stress, is observed in most diseases. In states of oxidative stress, vital macromolecules (proteins, nucleic acids) and lipids also suffer oxidative damage. Oxidative DNA damage, as well as exogenous insults (chemotherapeutic agents, ionizing radiation, UV radiation), trigger a coordinated response to avoid permanent genetic damage. The protein of focus in our research, poly(ADP-ribose) polymerase-1 (PARP-1), is a member of the PARP family of enzymes and is at the frontline of DNA breakage sensing by marking the site of DNA damage and recruiting DNA repair proteins. PARP-1, activated by DNA breakage, cleaves the energy substrate NAD+ molecule into ADP-ribose and nicotinamide, and from the former it produces branched poly(ADP-ribose) polymers to tag proteins in the vicinity of DNA breakage. This role in DNA damage repair is also heavily relied upon by tumor cells to evade various DNA-damaging anticancer therapies. The importance of the regulated function of PARP-1 enzymes is underlined by the observation that excessive PARP-1 activity is not necessarily associated with beneficial consequences. In the case of irreversible and severe DNA damage, excessive PARP-1 activation induces a cell death pathway, which plays a key role in cell death in e.g., myocardial infarction and cerebral vascular catastrophes (stroke). In addition to sensing DNA breaks, PARP-1 also has moonlighting functions, notably gene expression, e.g., transcriptional regulation of genes for inflammatory mediator proteins. This multifaceted biological function makes PARP-1 inhibitors have a wide therapeutic potential in the treatment of a number of diseases.

ISTVÁN HERNÁDI

Behavioural pharmacological „topmodels" in translational neuroscience: opportunities and challenges

The mission of our research is to understand and model the higher-order cognitive (cognitive) functions of the brain and the cellular and behavioural mechanisms underlying the natural decline and other disorders of cognition (dementias) associated with ageing, from rodents to primates and humans. Our research focuses on the development of computer-driven, automated, non-verbal cognitive test batteries on a common platform between species. In addition, cognitive dysfunctions are elicited by e.g., pharmacologically induced transient amnesia, or by naturally increased cognitive load. In the resulting behavioural models, we systematically investigate key processes in attention, working memory, and the highest executive functions. In the present talk, we will provide insights into our basic research and drug development studies that show the most cross-species understanding of human cognition and its diseased processes and to assess the performance-enhancing effects of pharmacological treatments. The long-term goal of our work is also to unravel the yet unknown brain mechanisms underlying neurocognitive decline, which may later play a crucial role in both the diagnosis and treatment of cognitive disorders and the development of new drug candidates.

LÁSZLÓ ACSÁDY

Neuronal basis of stress induced behavioral alterations

Following a traumatic event millions of people develop acute stress disorder (ASD) every year which, if it lasts longer than 30 days is called posttraumatic stress disorder (PTSD). The majority of stress research focused on PTSD but we have very little understanding what happens in the brain right after a single, intense stress event, like a street attack. Stress may affect dozens of brain centers at the same time or there may be a few hot spots which register the stress event and play a dominant role in establishing the stressed phenotype. Using a rodent model of ASD we identify a hub region within a subcortical structure called thalamus which fulfills the properties of a stress center. We show that in this structure a single stress event perturbs neuronal activity for a prolonged period (days) and leads to ASD, conversely, reducing the activity of this center for only one hour after the stress event prevents the development of ASD and normalize brain activity. Since the synaptic organization of this thalamic center is similar in mice and man we propose that the region may be critically involved in the establishing ASD in humans as well.

ANNA GEORGINA KOPASZ

A versatile transposon-based technology for the validation of potential cancer "driver" alterations in the mouse liver

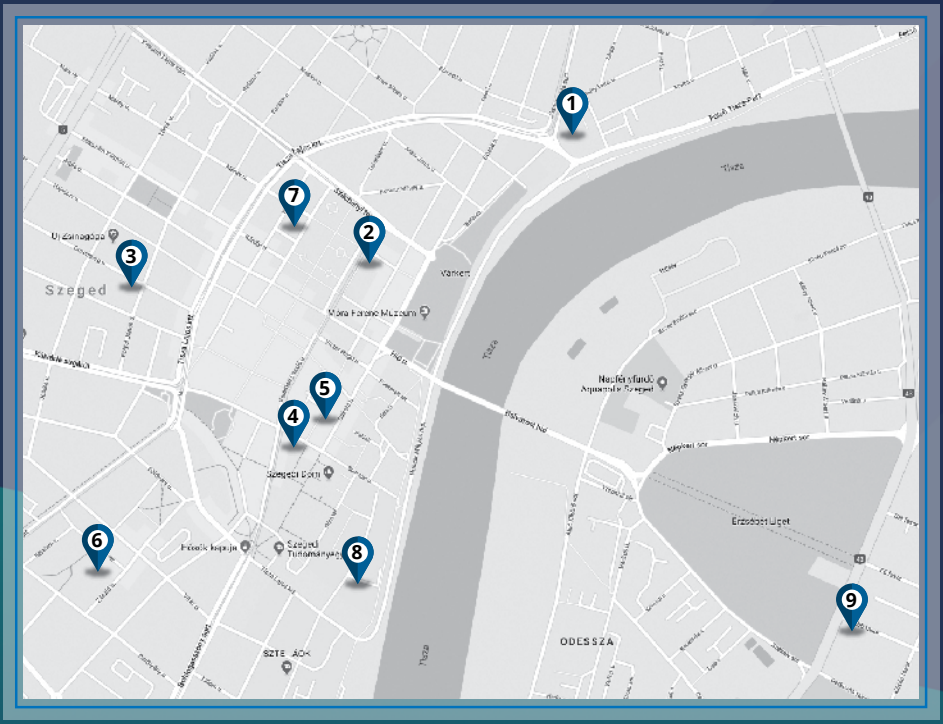
Nowadays, the greatest challenge of cancer research is the identification of "driver" mutations facilitating disease progression, among the more abundant "passenger" mutations found in tumors. Each and every gene with proven cancer "driver" role may open up new possibilities in the era of cancer treatment research. However, „driver" mutations with lower frequency cannot be identified alone using bioinformatics methods based on mutation frequency analysis. Thus, there is a growing demand for *in vivo* experimental systems where cancer "driver" roles may be confirmed.

By combining RNAi-based gene silencing and very efficient somatic transgenesis, we obtained an *in vivo* experimental system that allows analyzing the function of potential „driver" genes in the mouse liver. We ensured the equalized co-expression of the potential oncogene, the marker gene and the miRNA by using a well-balanced bidirectional promoter which was previously characterized in our laboratory.

To demonstrate the ability of our technology to induce hepatocellular carcinoma, we silenced the endogenous Tp53 and overexpressed an oncogenic hRas variant. The mutant Ras isoform alone triggers senescence in primary cells. Their transformation requires the silencing of a cooperative tumor suppressor, such as Tp53.

We believe that we established an accurate genetic model to study potential cancer "driver" candidates identified from large human cancer databases.

NOTES



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9. Biological Research Centre

Institutions participating in the implementation of the professional program of the National Academy of Scientist Education:

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