1. **Candidat**

Nume: Tomuleasa

Prenume: Ciprian

Doctor din anul : 2013

Pozitie ocupata: Cercetator Stiintific I – Centrul de Cercetare pentru Medicina Avansata Medfuture / Sef de Lucrari – Disciplina de Hematologie.

Institutia: Universitatea de Medicina si Farmacie Iuliu Hatieganu Cluj Napoca

Telefon mobil: (

Email:

2. **Editia "Gala Cercetarii Romanesti"**
3. **Premiul si Categoria pentru care se aplica: Individual**
4. **Lider de Echipa: -**
5. **Componenta Echipei de Cercetare: -**
6. **Descrierea a celor mai importante realizari stiintifice din ultimii 5 ani:**

A. **The youngest doctor in Romanian medical history, that has received the habilitation degree, allowing the grant director to coordinate Ph.D. theses, at the age of 32, having already coordinated 4 Ph.D. students, including on the management of ICU complications following allogeneic stem cell transplantation** (published in Kegyes et al, J Hematol Oncol 2022; Constantinescu et al, J Clin Medicine 2021; Constantinescu et al, J Immunother Cancer 2020).

B. **Joint research publications with a Nobel Prize laureate (Professor Aaron Ciechanover).**

a. KRAS/NRAS/BRAF mutations as potential targets in multiple myeloma. Sergiu Pasca, Ciprian Tomuleasa, Gabriel Ghiaur, Delia Dima, Vlad Moisoiu, Cristian Berce, Cristina Stefan, **Aaron Ciechanover**, Hermann Einsele. Frontiers in Oncology, 2019, 9:1137.

b. Targeting ubiquitination in myeloid malignancies. From basic research to drug discovery in MDS and AML. Rares Drula, Sabina Iluta, Diana Gulei, Delia Dima, Cristina Iuga, Anca Dana Buzoianu, Gabriel Ghiaur, **Aaron Ciechanover**, Ciprian Tomuleasa. Blood Reviews, 2022.

c. Insights into the roles of ubiquitin ligase KPC1: from cell cycle control to NF-kB regulator. Diana Gulei, Rares Drula, Gabriel Ghiaur, Anca Dana Buzoianu, Ciprian Tomuleasa, **Aaron Ciechanover**. Cancer Research, 2023.
d. The NF-kB subunit generated by KPC1-mediated ubiquitination and proteasomal processing suppresses tumor growth. Yelena Kravtsova-Ivantsiv, Gilad Goldhirsh, Ciprian Tomuleasa, Eli Pikarsky, **Aaron Ciechanover**. Cancer Cell International 2023.
e. Proteasome inhibition in combination with immunotherapies: state-of-the-art in multiple myeloma. David Kegyes, Diana Gulei, Rares Drula, Diana Cenariu, Bogdan Tigu, Delia Dima, Alina Tanase, Sorina Badelita, Anca-Dana Buzoianu, Stefan Ciurea, Gabriel Ghiaur, Evangelos Terpos, **Aaron Ciechanover**, Hermann Einsele, Ciprian Tomuleasa. Blood Reviews, 2023.

C. Member of the **World Health Organization Strategic Advisory Group of Experts on In Vitro Diagnostics** (Geneva, 2020).
D. **Organization of the Romanian ALL Group (RoALL)**, in collaboration with professor Alina Tanase (Fundeni Clinical Institute Bucharest) and Dr. Angela Dascalescu (Regional Institute of Oncology Iasi), to **implement the GMALL protocol for acute lymphoblastic leukemia, as well as reporting the data to the European LeukemiaNet** (professor Dieter Hoelzer) (2022).
E. **Organization of the National Registry for Hemophilia and Rare Coagulation Disorders**, in collaboration with the Romanian Society of Hematology, as a result of an international grant of the Novo Nordisk Haemophilia Foundation (2021)
F. The first publication of a Romanian team in Nature, as an editorial that supports the access to European Funding (**Horizon 2020: Funds to help Eastern Europe close the gap. Berce C, Tomuleasa C, Meza R. Nature. 2017;541(7636):157). This manuscript is an invited editorial, published by Nature – that publically asks the European Commission to support the access of Eastern European researchers to European research funding.**
G. 26 papers published in Q1 quartile, as main author. Annex 1 is attached.
H. Top 1% most cited authors.
I. 6 national and international reseacrh grants, each with a value of over 100.000 euro, as Shown in Chapter 9.

J. Cummulated influence scort of at least 5.

7. **Curriculum vitae narativ al candidatului:**

The project leader's scientific experience and publications demonstrate a profound background and expertise in the field of hematology and oncology, which is highly relevant to the proposed project on developing an antigen-specific T cell-based immune therapy for elderly, unfit acute myeloid leukemia (AML) patients. The expertise of Ciprian Tomuleasa in this domain is invaluable, and his contributions have significantly impacted the field of cellular therapies in Romania.

Ciprian Tomuleasa did his postdoctoral training in internal medicine at Ther Johns Hopkins Hospital in Baltimore, USA (2011-2013), a period when Johns Hopkins was ranked number 1 hospital in the United States for 21 consecutive years, probably being th best hospital in the world at the time. He did his training in stem cell transplantation at MD Anderson Cancer Center in Houston (2015, 2016), in which he was involved in phase I-III clinical trials on cellular therapies, stem cell transplantation and immune therapies (Biol Blood Marrow Transplant. 2016; Cancer. 2016). He was Romania's representative at the Lindau Nobel laureate Meeting, Lindau, Germany, July 2015. In February 2023, he was invited faculty at the Academic CAR T Cell Session – International Congress on CAR T cells (Rotterdam, The Netherlands), official meeting of the European Bone Marrow Transplantation Society.

Ciprian Tomuleasa has an impressive publication record closely related to the theme of the proposed project. Notably, he has published multiple articles that align with the objectives of the project. For instance, he achieved a remarkable milestone as a 4th-year medical student by successfully isolating the first cancer stem cell line in Romania in March 2010. Furthermore, he authored the pioneering report in Romania on chimeric antigen receptor (CAR) T cell-based immunotherapy for acute leukemia, which was published in Frontiers in Immunology in 2018 (Tomuleasa C, Fuji S, Berce C, et al.).

Additionally, Ciprian Tomuleasa has played a crucial role in the development of CAR T cell therapy in Romania. His leadership and involvement in a previous project, led by a team of young researchers, established the foundation for CAR T cell development in the country. The successful execution of the present project proposal is, therefore, built upon the accomplishments and prerequisites established by this earlier endeavor, research accepted for publication (Tigu et al, J Cell Mol Medicine, 2023, in press).

The project director's contributions extend beyond research articles. He has co-authored several books that focus on hematology and associated diseases. These books, published in both English and Romanian languages, have contributed to enriching knowledge in the field at both the national and international levels. For example, one publication titled "Nanopharmacology in Leukemia Chemotherapy," authored by Andrei Cucuianu, Ciprian Tomuleasa, Anca Bojan, Cristian Berce, Simion Astilean, and Emmet McCormack, serves as an important resource at the international level. Similarly, at the national level, the book "Leucemia mieloidă cronică de la terapia cu inhibitori de tirozin kinază la transplant" authored by Ciprian Tomuleasa, Delia Dima, and Adrian Trifa contributes significantly to the understanding and management of chronic myeloid leukemia.

The grant director coordonated 20 research or collaborative grants between 2011 and present, with a total funding of 2 million euro, including two research grants in collaboration with the United States (co-PI being professor Gabriel Ghiaur – Johns Hopkins University, investigating the tumor microenvironment of myelodysplastic syndromes), respectivvely a joint grant with Israel (co-PI being the 2004 Nobel Prize Laureate Aaron Ciechanover, investigating the role of NF-kB in cancer immunology of solid malignancies). The grant director also coordinated a previous national grant for Young Teams, which aimed to bring CAR T cell technology in the preclinical setting in Romania, a grant which allowed the first description (both in Romania as well as internationally) of a novel CAR T cell for acute megakaryoblastic leukemia.

8. **Lista publicatiilor individuale ale candidatului:**

- Annex 1 – Excell file.

9. Lista proiectelor de cercetare castigate de candidat:

10. No.	**Funding mechanism**	**Projects**	**Position**	**Period**	**Partner budget (EURO)**
1	Grant received after the Romania – European Economic Space (EES) International Research Grant	Nanotechnology approach in Acute Myeloid Leukemia management – Collaboration with Norway (University of Bergen) – acronym: **NanoLAM**	**Grant manager** for the partner institution - Ion Chiricuta Oncology Institute (**Principal**	2014-2016	110.000

	Competition 2014-2016		**investigator – Prof. Andrei Cucuianu, Iuliu Hatieganu University of Medicine and Pharmacy Cluj Napoca). Co-principal investigator: Prof. Emmet McCormack – University of Bergen, Norway**		
2	Internal Grant Competition of the Iuliu Hatieganu University of Medicine and Pharmacy, for young researchers, 2014-2015	Cell and molecular mechanisms of primary myelofibrosis	**Principal investigator -** Iuliu Hatieganu University of Medicine and Pharmacy	2014-2015	8.000
3	Grant received after the Romania– European Economic Space (EES) International Grant Competition 2015-2016	Innovative Nanoparticles-based Chemotherapy for Acute Myeloid Leukemia - Collaboration with Norway (University of Bergen) – acronym: **NanoChemotherapy**	**Principal investigator-** Iuliu Hatieganu University of Medicine and Pharmacy. **Co-principal investigator: Prof. Emmet McCormack – University of Bergen, Norway**	2015-2016	41.000
4	Grant received after the Young Research Team Competition,	Massively parallel high-throughput DNA sequencing for the identification of	**Principal investigator-** Iuliu Hatieganu University of	2016-2017	125.000

	awarded by the Romanian Research Ministry and Education 2016-2017	microRNAs differentially expressed between the metastatic site and the tissue of origin in cancers of unknown primary site	Medicine and Pharmacy		
5	Internal Grant Competition of the Iuliu Hatieganu University of Medicine and Pharmacy, for medical students, 2015-2016	A synthetic lethality approach in the acute myeloid leukaemia chemotherapy: PARP inhibitors plus anthracycline plus decitabine vs anthracycline plus decitabine –in vitro efficacy testing	**Grant mentor** for Grigore Gafencu	2015-2016	2.000
6	Internal Grant Competition of the Iuliu Hatieganu University of Medicine and Pharmacy, for medical students, 2015-2016	The efficacy of pirfenidone in primary myelofibrosis	**Grant mentor** for Sonia Selicean	2016-2017	2.000
7	Grant received after the Romania - P.R. China International Bilateral Collaboration competition 2016-2017	Invasive biomarkers for graft versus host disease following bone marrow hematopoietic stem cell transplantation	**Principal investigator-** Iuliu Hatieganu University of Medicine and Pharmacy. **Co-principal investigator: Prof. Jianlian Shen – Navy General Hospital, Beijing, China**	2016-2017	9.533
8	Grant received after the FDI competition of the National Council for the Financing	Modern training for healthcare professionals affiliated to the departments of hematology, oncology	**Principal investigator-** Iuliu Hatieganu University of	2017	43.826

	of University Education 2017	and bone marrow transplantation	Medicine and Pharmacy		
9	Grant received after the FDI competition of the National Council for the Financing of University Education 2018	Correlation of the educational curricula in molecular medicine and translational onco-hematology with the European workforce demand	**Principal investigator-** Iuliu Hatieganu University of Medicine and Pharmacy	2018	38.922
10	Grant received from the National Research Ministry for Frontiers Research 2017-2022	Multifunctional magnetoplasmonic nanoparticles for point of care applications in acute myeloid leukemia, acronym: NanoTEX	**Grant manager** for Ion Chiricuta Oncology Institute. **(Principal investigator: Prof. Emil Burzo, Babes Bolyai University Cluj Napoca, Romania)**	2018-2022	180.000 (total grant value – 1.800.000)
11	Invited Professor 2018 Grant – Gabriel Ghiaur, Johns Hopkins University School of Medicine, from the National Research Ministry	Invited Professor Grant – Gabriel Ghiaur, Johns Hopkins University School of Medicine.	**Principal investigator,** for the Iuliu Hatieganu University of Medicine and Pharmacy.	2018	2.619
12	Grant received after the Romania - P.R. China International Bilateral Collaboration competition 2018-2019	Experimental Immunotherapy for hematological malignancies	**Principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy. **Co-principal investigator: Prof. Liren Qian, Navy General**	2018 - 2019	8.609

			Hospital, Beijing, China		
13.	Grant received after the FDI competition of the National Council for the Financing of University Education 2019	Increase of the competitivity of medical education by correlating the curricula to Anglo-Saxon standards	**Principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy	2019	41.916
14.	Grant received after the Romania–European Economic Space (EES) International Grant Competition – Collaboration with Iceland; 2020-2022	HE-RO-IS strategic collaboration in hematology – Iceland collaboration (Reykjavik University) – Acronym: **HERO**	**Principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy. **Co-principal investigator: Prof. Olafur Eysteinn Sigurjonsson, Reykjavik University, Iceland**	2020 - 2021	144.153
15.	Novo Nordisk Haemophilia Foundation International Grant 2020-2022	Strengthen haemophilia care in the north and establish a national registry in Romania – Romania 3	**Principal investigator,** Romanian Hematology Society	2020 - 2021	81.903
16.	Grant received from the National Research Ministry for Postdoctoral Research 2020-2022	Evaluation of the effect of human chorionic gonadotrophin in stem cell transplantation as a new method of pretransplant mobilization	**Grant mentor for Andrei Cismaru - MD, PhD,** Iuliu Hatieganu University of Medicine and Pharmacy	2020 - 2022	51.667
17.	Grant received from the National Research Ministry for Postdoctoral	New generation preclinical model for evaluating the therapeutic role of microRNA-505-	**Grant mentor for Diana Gulei - PhD,** Iuliu Hatieganu University of	2020 - 2022	51.667

	Research 2020-2022	5p for metastasis limitation in melanoma	Medicine and Pharmacy		
18.	Grant received from the National Research Ministry for Young Research Teams 2020-2022	Supporting a team of young researchers in creating an independent research program based on the use of the Sleeping Beauty protocol for developing CAR T cells – Acronym: **SEATTLE**	**Principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy	2020 - 2022	93.001
19.	Grant received after the Romania – Wallonia/Belgium International Bilateral Collaboration competition 2020-2022	Consolidation of the Wallonia-Romania collaboration for setting of new standard operation procedures (SOP) in immunotherapy	**Principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy. Co-principal investigator: **Prof. Jo Caers, University of Liege, Belgium**	2021-2022	10.561
20.	Grant received from the National Research Ministry for Exploratory Research 2020-2023	Harnessing the ubiquitin-proteasome system (UPS) to suppress tumor's growth via manipulating generation of NF-kB – Acronym: **ROME**	**Co-principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy. **Principal investigator: Prof. Aaron Ciechanover – Nobel Prize in Chemistry 2004**	2021-2024	250.000
21.	Grant received from the National Research Ministry for Exploratory Research 2020-2023	The role of stromal CYP26 in retinoid homeostasis in the context of myelodysplastic syndromes pathogenesis	**Co-principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy. **Principal**	2021 - 2024	250.000

		and response to treatment Acronym: **LONDON**	**investigator: Prof. Gabriel Ghiaur**		
22.	Novo Nordisk Haemophilia Foundation International Grant 2022-2024	Strengthen haemophilia care in the north-eastern part of Romania and in Moldova and establish a registry in Moldova – Romania 4	**Principal investigator,** Romanian Hematology Society	2022 - 2024	102.779
23.	Grant received from the National Health Ministry, for providing outreach healthcare services to vulnerable population from isolated areas 2022-2023	Sequencing as standard-of-care in diagnosis of hemophilia and rare coagulation disorders in Romania	**Principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy. Grant director: Romanian Hemophilia Association (Mr. Daniel Andrei)	2022 - 2023	222.222
24.	Grant received from the Romanian Academy of Science	Mathematical model for clonal hematopoiesis	**Principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy.	2023-2024	10.000
25.	Grant received from the European Hematology Association	CAR NK-cells for tumor-associated macrophage immunomodulation – a new era of immunotherapy	**Principal investigator,** Iuliu Hatieganu University of Medicine and Pharmacy.	2024	20.000
Total amount of continuous funding between 2014 - present					**1.901.378 EURO**