Progress and Challenges in Cancer Immune Therapy

European Training Network Immutrain

From Tuesday 23th to Friday 26th July 2019

Melchor Fernández Almagro, 3. 28019 Madrid









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Editorial

Dear guests,

Welcome to the conference "Progress and challenges in cancer immune therapy. Experience of the European Training Network Immutrain"

This is the closing symposium of a series of four international congresses framed within the Marie Skłodowska-Curie training program "Immutrain – Immunotherapy of Cancer". Starting in 2015, our main objective was to build a competitive network of laboratories across Europe interested in immune modulation in cancer. Since then, ten academic research groups and five industrial partners from nine countries have worked together to promote career development of fifteen young (early stage) research investigators. Our distinctive feature is our interest in gene discovery and drug development, particularly in the context of state-of-the-art immunomodulatory antibodies and anticancer agents based on dsRNA.

Progress has been remarkable in these few years. Work by our Early Stage Researchers has been able to identify tumor-secreted factors that favor immune suppression, uncover immune checkpoints, generate antibodies against new targets and ultimately, devise strategies to reactivate the immune system and reduce cancer growth and metastasis. Eleven co-authored original papers have been published and three patent applications have been submitted.

This conference aims to present achievements of *Immutrain*, as well as to reflect on "what is next" in the field of immunotherapy. There will be talks by group leaders of *Immutrain*, selected young researchers of the network and international leaders on immunology and tumor progression.

The last two days of the conference will be dedicated to various soft skills that are also key elements in the training of our early research investigators. To this end, we have invited journal editors, pharmaceutical industry, entrepreneurs, investors and patent specialists to present their work experience and discuss challenges related to innovation, business and dissemination of knowledge. Afterwards, our early research investigators will have one-to-one meetings with these experts in a closed session to explore how to take advantage of the scientific and personal knowledge gained through the *Immutrain* network, and to learn about career opportunities.

Proud of how *Immutrain* has contributed to advancing basic and translational research by all involved, we wish you a productive conference!

Marisol Soengas

Project Leader of Immutrain
Spanish National Cancer Research Center, CNIO.







Quo vadis cancer immune therapy? Current status and future challenges of research development in Europe

"It is not a breakthrough, it's a revolution" this is how an oncologist termed cancer immunotherapy opening a conference in Munich last year. Indeed, the advances of targeting the immune system for the benefit of patients suffering from cancer have been breathtaking: the number of tumor entities with proven prolonged — and sometimes long-term — survival upon treatment with check-point inhibitors is steadily growing. And we are better understanding the mechanisms of adoptive CAR T cell therapy which will lay the foundations to extend its success to non-hematological malignancies.

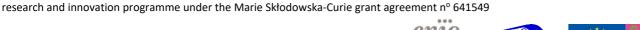
Yet, major challenges remain: First, the unwanted effects of immunotherapy – cytokine release syndrome, neurological toxicity and autoimmune complications – require highly specialized and interdisciplinary patient care, sometimes including intensive care medicine. Second, the high costs – both in treatment burden and in financial terms – make the identification of predictive biomarkers paramount; they are necessary to identify those patients suffering from tumors that will respond to a given tumor immunotherapy with reasonable probability. And third, society and public health policy will need to identify policies to best allocate these costly therapies to the appropriate patients.

With these challenges, world-wide efforts are on the way: just for the example of CAR T cell-based therapies, tenfold more clinical studies are currently ongoing both in the US and in East Asian countries compared to all European countries together. This underlines the need for EU countries to join forces, to intensify collaborations and to set common standards.

Immutrain was established in 2015. It has brought together a ten academic research groups — and five industrial partners— from nine European countries closer together. Fifteen young researchers have started a scientific career in the field of tumor immunotherapy. Their experimental expertise and their exposure to the field will make them invaluable research team members, both in academia and in biotech and pharmaceutical industry. As the coordinator of the network I sincerely thank these young scientists, the responsible principle investigators — in the UK, Netherlands and Denmark, in France, Spain and Italy, in Switzerland, Austria and Germany — and the fantastic coordinating team for their great commitment over the past four years. This has been an extraordinary experience, both on a scientific and on a personal level.

Stefan Endres

Coordinator of Immutrain Ludwig-Maximilians-Universität Munich





This conference is organised by Centro Nacional de Investigaciones Oncológicas and funded by the European Union's Horizon 2020





Immutrain, four years of training and research in cancer immune therapy on European level

Immutrain is the first European training program dedicated to the immunotherapy of cancer. It aims at tackling major challenges: incomplete understanding on the mechanisms by which tumors evade immune surveillance, and to improve the efficacy of the antibody-based therapies. Although significant progress has been achieved, only a fraction of the patients responds to treatment. Resistances to classical antibody therapies arise from local effector suppression, from loss of antigen or from inhibitory effects on signaling pathways. To avoid or bypass these resistance mechanisms, the scientists of Immutrain combine antibodies with several immunotherapeutic approaches: adoptive T cells, immune cell activation, dendritic cell therapy and nucleic acids. These antibodies have been combined with alternative immunostimulatory agents to ultimately increase antitumor efficacy by enhancing specificity and decreasing secondary toxicities. To this end, the work packages of Immutrain were set in an ambitious manner to address four most promising strategies to enhance the clinical efficacy of antibodies:

- ❖ Work package 1, "Combination of antibodies with adoptive T cell transfer", to increase the infiltration of tumor-specific T cells to tumor sites.
- ❖ Work package 2, "New formulations and combinations of antibodies to activate immune cells", with the objective of restoring immune activating mechanisms.
- Work package 3, "Combination of antibodies with dendritic cell therapy", to unleash dendritic cell-induced immune responses.
- ❖ Work package 4, "Target discovery and validation for antibody combination therapies", designed to improve the delivery and efficacy of immunostimulatory nucleic acids.

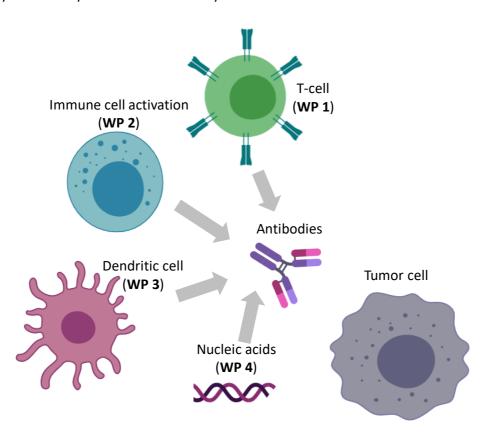


Fig. 1 The work packages of Immutrain







To reach its scientific objective, the network has brought together 19 experts from the fields of tumor biology, monoclonal antibodies, dendritic cells, T-cells and immunomodulatory nucleic acids with a considerable industrial involvement.

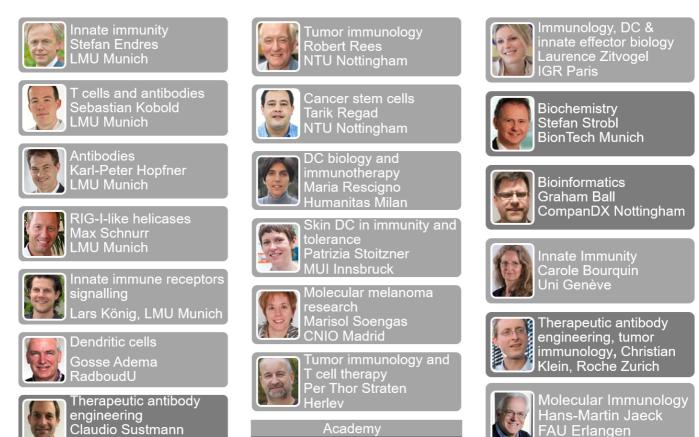


Fig. 2 Expertise of the project leaders of Immutrain

Roche Munich

As a large-sized network, *Immutrain* tackled one of the major threats to Europe's progress in cancer research and treatment: the regional fragmentation and the limited number of multidisciplinary and transnational collaborations. The academic and industrial laboratories coordinated their efforts to develop a training program for PhD students, so called Early Stage Researchers.

Industry

This program has combined training to foster scientific and interpersonal skills. Actions have been implemented at two levels: (i) locally, where each student has been enrolled in a graduate school and has conducted a PhD project in a partner lab and (ii) at the European level: twice a year, the Early Stage Researchers have presented their work-progress and met all the members at a conference and a workshop.

Five key thematic priorities structure the contents of the European training:

- Overview of immunologic combination partners for antibodies
- How to develop new therapies (target validation, drug discovery and development)
- Methodological know-how in the field of immunotherapy
- Transferable skills: scientific writing, how to communicate science, science and diversity, work life balance, intellectual property and patent filing, transfer of technology, oral and poster presentation,
- To improve chances of cooperation and employment in industry and academy: mentoring program and networking activities.







Since December 2015, six workshops and four conferences have taken place in Munich, Milan, Copenhagen, Paris, Nijmegen and Madrid to cross-fertilize the know how gained in the network. At these occasions, the students met more than 100 guest-speakers and took part in more than 20 sessions on methods, soft-skills and career development.

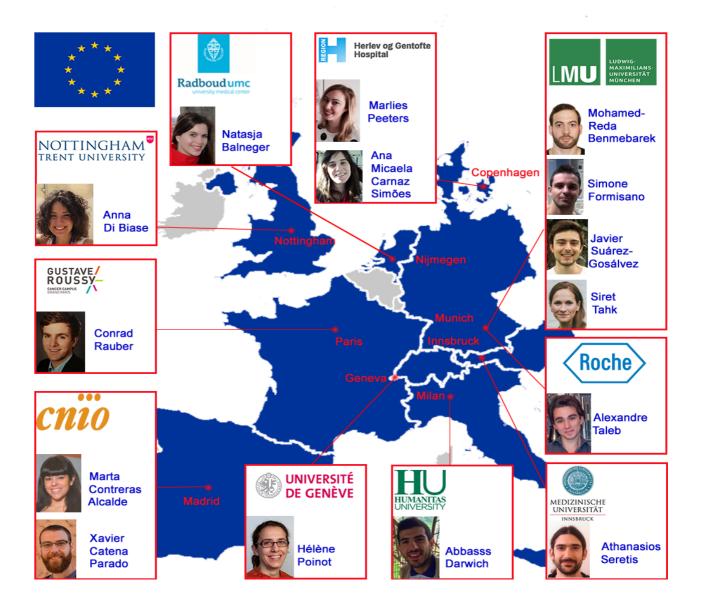


Fig. 3 Early Stage Researchers of Immutrain

Immutrain responded to the need for well-trained experts in the field, capable of recognizing opportunities of the most recent scientific developments and to translate them into therapies. In particular, in the light of a vivid market of biomedical and pharmaceutical enterprises, we focused also on technology transfer as valuable knowledge for young professionals. The young research investigators have benefited of an intensive exchange of ideas, experiences and methods that have allowed them to become highly competitive in the field of immunotherapy of cancer.

Sebastian Kobold

Scientific Coordinator of Immutrain Ludwig-Maximilians-Universität Munich







Publications of Immutrain

Early Stage Researchers as co-authors are marked in blue and Project Leaders in black

Original papers

2019

11. Peeters MJW, Dulkeviciute D, Draghi A, Ritter C, Rahbech A, Skadborg SK, Seremet T, Carnaz Simoes AM, Martinenaite E, Halldórsdóttir HR, Andersen MH, Olofsson GH, Svane IM, Rasmussen LJ, Met O, Becker JC, Donia M, Desler C and thor Straten P.

MERTK acts as a costimulatory receptor on human CD8+ T cells American Association for Cancer Research 2019 JIF 10.2

10. Karches CH, **Benmebarek MR**, Schmidbauer ML, Kurzay M, Klaus R, Geiger M, Rataj F, Cadilha BL, Lesch S, Heise C, Murr R, vom Berg J, Jastroch M, Lamp D, Ding J, **Duewell P**, Niederfellner G, **Sustmann C**, **Endres S**, **Klein C** and **Kobold S**.

Bispecific antibodies enable synthetic agonistic receptor-transduced T cells for tumor immunotherapy Clinical Cancer Research 2019; in press JIF 10.2

9. Liu X, Li J, Cadilha B, Markota A, Voigt C, Huang Z, Lin P, Wang D, Juncheng D, Kranz G, Krandick A, Libl D, Zitzelsberger H, Zagorski I, Braselmann H, Pan M, Zhu S, Huang Y, Niedermeyer S, Reichel Ch, Uhl B, Briukhovetska D, Suarez Gosalvez J, Kobold S, Gires O, Wang H.

Epithelial-type systemic breast carcinoma cells with a restricted mesenchymal transition are a major source of metastasis.

Science Advances 2019; in press.

JIF 11.5

8. Heise T, Pijnenborg JFA, Büll C, van Hilten N, Kers-Rebel ED, **Balneger N**, Elferink H, **Adema GJ**, Boltje TJ. Potent metabolic sialylation inhibitors based on C-5-modified fluorinated sialic acids. *Journal of Medicinal Chemistry* 2019 Jan 24;62(2):1014-1021

JIF 6.3

2018

7. Büll C, Boltje TJ, **Balneger N**, Weischer SM, Wassink M, van Gemst JJ, Bloemendal VR, Boon L, van der Vlag J, Heise T, den Brok MH, **Adema GJ**.

Sialic acid blockade suppresses tumor growth by enhancing T-cell-mediated tumor immunity. *Cancer Research* 2018; 78(13):3574-3588

JIF 9.1

6. Vadakekolathu J, Al-Juboori SIK, Johnson C, Schneider A, Buczek ME, **Di Biase A**, Pockley AG, Ball GR, Powe DG, **Regad T**.

MTSS1 and SCAMP1 cooperate to prevent invasion in breast cancer.

Cell Death Disease 2018; 9(3):344.

JIF 4.6

5. Rataj F, Kraus FBT, Chaloupka M, Grassmann S, Heise C, Cadilha B, Duewell P, Endres S, Kobold S.

PD1-CD28 fusion protein enables CD4+ T cell help for adoptive T cell therapy in models of pancreatic cancer and non-Hodgkin-lymphoma.

Frontiers in Immunology 2018; 9:1955.

JIF 5.5







4. Routy B, Le Chatelier E, Derosa L, Duong CPM, Alou MT, Daillère R, Fluckiger A, Messaoudene M, Rauber C, Roberti MP, Fidelle M, Flament C, Poirier-Colame V, Opolon P, Klein C, Iribarren K, Mondragón L, Jacquelot N, Qu B, Ferrere G, Clémenson C, Mezquita L, Masip JR, Naltet C, Brosseau S, Kaderbhai C, Richard C, Rizvi H, Levenez F, Galleron N, Quinquis B, Pons N, Ryffel B, Minard-Colin V, Gonin P, Soria JC, Deutsch E, Loriot Y, Ghiringhelli F, Zalcman G, Goldwasser F, Escudier B, Hellmann MD, Eggermont A, Raoult D, Albiges L, Kroemer G, Zitvogel L. Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors. *Science* 2018; 359(6371):91-97.

JIF 41.0

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Generation of in vitro model of Epithelial Mesenchymal Transition (EMT) via the expression of a cytoplasmic mutant form of PML.

Cancer Stem Cells: Methods and Protocols 2018;1692:129-138. JIF 3.2

2017

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Whole-body imaging of lymphovascular niches identifies pre-metastatic roles of midkine. *Nature* 2017; 546(7660):676-680. JIF 44.9

1. Voigt C, May P, Gottschlich A, Markota A, Wenk D, Gerlach I, Voigt S, Stathopoulos GT, Arendt K, Heise C, Rataj F, Janssen KP, Königshoff M, Winter H, Himsl I, Thasler W, Schnurr M, Rothenfußer S, **Endres S, Kobold S**.

Cancer cells induce interleukin-22 production from memory CD4+ T cells via interleukin-1 to promote tumor growth. *Proceedings of the National Academy of Sciences* 2017; 10:1073.

JIF 9.6

Reviews

2019

JIF 4.4

4. Stoiber S, Cadilha BL, **Benmebarek MR**, Lesch S, **Endres S, Kobold S.**Limitations in the design of chimeric antigen receptors for cancer therapy.

Cells 2019 May 17;8(5)

JIF 4.8

3. **Benmebarek MR**, Karches CH, Cadilha BL, Lesch S, **Endres S, Kobold S**. Killing mechanisms of chimeric antigen receptor (CAR) T Cells. *International Journal of Molecular Sciences* 2019 Mar 14;20(6). JIF 3.9 2018

2. Gottschlich A, Endres S, Kobold S.

Can we use interleukin-1 β blockade for lung cancer treatment? Translational Lung Cancer Research 2018;7(Suppl 2):S160-S164. JIF 1.8

1. Kobold S, Pantelyushin S, Rataj F, vom Berg J.

Rationale for combining bispecific T cell activating antibodies with checkpoint blockade for cancer therapy. *Frontiers in Oncology* 2018; 8:285.







Program

15:30 - 15:50

Tuesday July 23	th , 2019
12:30	Registration
13:30 - 13:50	Welcome address
	María Soengas, Spanish National Cancer Research Center, Madrid and
	Stefan Endres, Ludwig-Maximilians-Universität München
14:00 - 14:30	Sebastian Kobold, Ludwig-Maximilians-Universität München
	Strategies to enable adoptive t cell therapy of cancer
14:30 - 15:00	Tarik Regad, Nottingham Trent University
	Development of antibody-based therapy against aggressive prostate cancer
15:00 – 15:30	Manuel Valiente, Spanish National Cancer Research Center, Madrid
15.00 15.50	The potential of astrocytes as immune modulators in brain tumors
15:30 – 16:00	Coffee break
15.50 – 10.00	Cojjee break
16:00 – 16:30	Karl-Peter Hopfner, Ludwig-Maximilians-Universität München
	Multifunctional antibodies combining tumor targeting and immune checkpoint blockade
16:30 – 17:00	Patrizia Stoitzner, Medical University of Innsbruck
	Dendritic cell based immunotherapy to overcome resistance to tumor targeted therapy with BRAF
	inhibitor
17:00 – 17:30	Hector Peinado, Spanish National Cancer Research Center, Madrid
	Tumor-Immune Microenvironment crossregulation during tumor progression
17:30 - 18:00	Coffee break
18:00 - 18:20	Mohamed-Reda Benmebarek, Ludwig-Maximilians-Universität München
	Bispecific antibodies drive synthetic agonistic receptor transduced T cells for cancer
	immunotherapy
18:20 - 18:50	Gregor Hutter, Universitätsspital Basel
	Novel immunotherapeutic strategies for the treatment of gliomas
20:00 – 22:00	Welcome Cocktail and Dinner with speakers
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Wednesday Jul	y 24 th , 2019
09:00 - 09:20	Per thor Straten, University Hospital Herlev
	The exercise of TAMing the immune system
09:30 - 10:00	Maria Rescigno, Humanitas University, Milan
	Microbiota in cancer progression
10:00 - 10:30	Coffee break
10:30 - 11:00	Siret Tahk, Ludwig-Maximilians-Universität München
10.50 11.00	Evaluation of the bifunctional SIRPα-anti-CD123 fusion antibody for the elimination of acute
	myeloid leukemia stem cells
11:00 – 11:30	Lars König, Ludwig-Maximilians-Universität München
11.00 – 11.50	
11.20 12.00	Noncanonical cell death induction by dsRNA independent of RIG-I-like receptors
11:30 – 12:00	Nabil Djouder, Spanish National Cancer Research Center, Madrid
	Targeting IL-17A signaling in metabolic disorders and HCC
12.00 45.00	Long the base of a graph of Companies and December 1997 of the state o
12:00 – 15:00	Lunch break and parallel Supervisory Board Meeting of Immutrain in closed session
45.00 45.00	
15:00 – 15:30	Eugene Maraskovsky, CSL Limited, Melbourne, Australia
	Challenges in optimising strategies for the treatment of cancer

This conference is organised by Centro Nacional de Investigaciones Oncológicas and funded by the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement nº 641549

Identification of Chitinase 3-like 1 protein as a soluble immune checkpoint

Abbass Darwich, Humanitas University, Milan







16:00 – 16:20	Claudio Sustmann, Roche Innovation Center Munich Tackling complex biologies with advanced antibody engineering
16:30 – 16:50	Carole Bourquin, University of Geneva
	Tumor-derived HMGB1 controls the anticancer immune response
17:00 – 17:30	Coffee break
17:30 – 17 :50	Hans-Martin Jäck, Friedrich-Alexander-Universität Erlangen-Nürnberg
	A transgenic mouse platform to produce therapeutic human monoclonal antibodies
18:00 - 18:20	María Soengas, Spanish National Cancer Research Center
	Dissecting the interplay between tumor cells and the immune system in melanoma progression and response to therapy

Thursday July 25th, 2019

09:00 – 13:00	Meet the experts in the field of publishing, patent, biotech and investment This session will present the work and experience of different experts
09:00 – 9:20	Patricia Salama, EU Patent Specialist, Elzaburu
09:30 – 09:50	Joao Monteiro, Editor, Nature Medicine
10:00 – 10:20	Gema Fuerte Hortigón, European Field Application Scientist, MissionBio
10:30 – 11:00	Coffee break
11:00 - 11:20	Tamara Maes, CSO, Oryzon Genomics
11:00 – 11:20 11:30 – 11:50	Tamara Maes, CSO, Oryzon Genomics Raúl Martín-Ruiz, Partner, Ysios Capital
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11:30 – 11:50	Raúl Martín-Ruiz, Partner, Ysios Capital
11:30 – 11:50 12:00 – 12:20	Raúl Martín-Ruiz, Partner, Ysios Capital Julen Oryazabal, Partner, Columbus Venture Partners

Thursday July 25th, 2019 – Closed section for Immutrain's members

14:00 – 19:30	ESR elevator pitches
	In this session, the students will present their projects in front of the experts.
	Elevator pitch: 5 min presentation + 5 min questions and comments
14:00 - 14:10	Xavier Catena, Spanish National Cancer Research Center, Madrid
14:15 – 14:25	Marta Contreras, Spanish National Cancer Research Center, Madrid
14:30 - 14:40	Simone Formisano, Ludwig-Maximilians-Universität München
14:45 – 14:55	Hélène Poinot, University of Geneva
15:00 - 15:10	Conrad Rauber, Institut Gustave Roussy, Paris
15:15-15:45	Coffee break
15:45 – 15:55	Athanasios Seretis, Medical University of Innsbruck
16:00 - 16:10	Natasja Balneger, Radboud University Medical Center
16:15 – 16:25	Abbass Darwich, Humanitas University, Milan
16:30 – 16:40	Alexandre Taleb, Roche Innovation Center Munich
16:45 – 16:55	Siret Tahk, Ludwig-Maximilians-Universität München
17:00-17:30	Coffee break
17:30 – 17:40	Ana Micaela Carnaz Simões, University Hospital Herlev
17:45 – 17:55	Marlies Peeters, University Hospital Herlev
18:00 - 18:10	Anna Di Biase, Nottingham Trent University
18:15 – 18:25	Mohamed-Reda Benmebarek, Ludwig-Maximilians-Universität München
18:30 – 18:40	Javier Suarez-Gosalvez, Ludwig-Maximilians-Universität München







Friday July 26th, 2019 – Closed session for Immutrain's members

09:00 – 13:30 *Meet the experts: one to one*

In this session, the students will meet for 15 minutes individually with:

Patricia Salama, EU Patent Specialist, Elzaburu

Gema Fuerte Hortigón, European Field Application Scientist, MissionBio

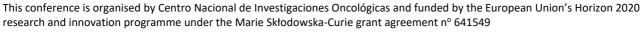
Joao Monteiro, Editor, Nature Medicine

Raúl Martín-Ruiz, Ysios Capital

Julen Oryazabal, Partner, Columbus Venture Partners **Ana B Irigaray**, Regulatory Affairs Director, Pharmamar

We will make a break of 30 minutes

13:30 – 14:00 *Closing remarks*









Speakers



Mohamed-Reda Benmebarek

- •Ludwig-Maximilians-Universität, Germany
- Early Stage Researcher, Division of Clinical Pharmacology



Carole Bourquin

- •University of Geneva, Switzerland
- Professor of Pharmacology
- Group leader Immunopharmacology of Cancer



Abbass Darwich

- Humanitas University, Italy
- Early Stage Researcher of Immutrain



Nabil Djouder

- •Spanish National Cancer Research Center, Spain
- Junior Group Leader, Group of Growth factors, Metabolism and Cancer



Stefan Endres

- •Ludwig-Maximilians-Universität, Germany
- Head, Division of Clinical Pharmacology
- Coordinator of Immutrain



Karl-Peter Hopfner

- •Ludwig-Maximilians-Universität, Germany
- •Director, Gene Center and Division of Biochemistry
- •Group leader of Structural Molecular Biology









Gregor Hutter

- University Hospital Basel, Switzerland
- Attending Physician, Neurosurgery
- Research Group Leader, Brain Tumor Immunotherapy Lab



Hans-Martin Jäck

- Friedrich-Alexander Universität Erlangen-Nürnberg, Germany
- Head, Division of Molecular Immunology



Sebastian Kobold

- •Ludwig-Maximilians-Universität, Germany
- •Group leader of Immunopharmacology, Division of Clinical Pharmacology
- Scientific coordinator of Immutrain



Lars König

- •Ludwig-Maximilians-Universität, Germany
- •Group leader of Cancer Vaccine Lab, Division of Clinical Pharmacology



Eugene Maraskovsky

- •CSL Limited, Melbourne, Australia
- •Executive Director, Head of Cell Biology & Physiology Department



Héctor Peinado

- •Spanish National Cancer Research Center, Spain
- •Head of Microenvironment and Metastasis Group









Tarik Regad

Nottingham Trent University, UK

•Senior Research Fellow, the John van Geest Cancer Research Centre



Maria Rescigno

- Humanitas University, Italy
- •Full Professor Pathology
- •Group Leader Mucosal immunology and microbiota Unit



María Soengas

- •Spanish National Cancer Research Center, Spain
- •Head of the Melanoma Group



Patrizia Stoitzner

- •Medical University of Innsbruck, Austria
- •Head of the Langerhans Cell Research Lab, Department of Dermatology, Venereology & Allergology



Claudio Sustmann

- •Roche Diagnostics GmbH, Germany
- •Head Program Management & External Innovation; Large Molecule Research



Siret Tahk

- •Ludwig-Maximilians-Universität, Germany
- Early Stage Researcher, Gene Center, Division of Biochemistry, Group of Structural Molecular Biology









Per thor Straten

- Hospital Herlev, Copenhagen University, Denmark
- Director, Center for Cancer Immunotherapy



Manuel Valiente

- •Spanish National Cancer Research Center, Spain
- •Head of Brain Metastasis Group

Experts



Gema Fuerte Hortigón

- MissionBio
- •European Field Application Scientist



Ana B Irigaray

- Pharmamar
- •Regulatory Affairs Director



Tamara Maes

- Oryzon Genomics
- •CSO







Raúl Martín-Ruiz

- •Ysios Capital
- Partner



Joao Monteiro

- •Nature Medicine
- Editor



Julen Oryazabal

- •Columbus Venture Partners
- Partner



Patricia Salama

- Elzaburu
- •EU Patent Specialist





To follow

Contact the Early Stage Researchers and the Project Leaders on LinkedIn IMMUTRAIN or go to www.immutrain.eu

Acknowledgements of the coordination team

We would like to thank very warmly all members of Immutrain and all the co-workers from the scientific, technical and administrative teams who supported the implementation of the project.

Our particular thanks go to the project leaders who organized European training events at their institution: Marisol Soengas, Madrid, from 23rd to 26th July 2019; Gosse Adema, Nijmegen, from 26th February to 1st March 2019; Laurence Zitvogel, Paris, from 2nd to 6th July 2018; Per thor Straten, Copenhagen, from 2nd to 6th October 2017 and Maria Rescigno, Milan, from 8th to 10th February 2017.

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And last but not least, we thank very much the members of the External Advisory Board who sent us assessments on progress of work: Ulrich von Andrian, Harvard Medical School; Charles Dinarello, University of Colorado and Radboud University; Heiner Igel, Ludwig-Maximilians-Universität Munich; Eugene Maraskovsky, CSL Limited, Melbourne and Kai Wucherpfennig, Harvard Medical School.

Simone Gautier, **Project Manager** Stefan Endres, Coordinator

Sebastian Kobold, Scientific Coordinator





