

MARIA THEMELI MD PhD

PERSONAL INFORMATION

Surname: **THEMELI**
Name: **MARIA**

PROFESSIONAL EXPERIENCE

July 2017-

To date: Assistant Professor. Department of Hematology, Amsterdam University Medical Centers, Location VUmc, Cancer Center Amsterdam.

July 2015-

July 2017: Senior Research Fellow. Marie Sklodowska Curie Fellow at VU Medical Center, Cancer Center Amsterdam. Supervisor: Dr. Tuna Mutis.

Jan 2010-

June 2015: Post-doctoral Research Fellow
Center for Cell Engineering at Memorial Sloan-Kettering Cancer Center.
Mentor: Dr. Michel Sadelain MD PhD

EDUCATION

Oct 2006-

Sept 2011: PhD candidate
University of Patras Medical School.
Mentor: Prof. Alexandros Spyridonidis.
Thesis: "Mechanism and clinical significance of genomic instability after Hematopoietic Cell Transplantation."

Oct 2000-

Aug 2006: Medical Degree
Patras University Medical School. Graduation with MD degree: 11th August 2006. Grade: 8,14/10 (equivalent to: Summa Cum Laude). Top 2-3% of the students who have graduated the last 10 years and 1st between the 2006 graduates.

PROFESSIONAL LICENSURE

Achaia Province, Greece 2009 E2/4984/6-6-1996

HONORS AND AWARDS

- 2017-2019: Cancer Center Amsterdam Fellowship for junior group leader.
- 2015-2017: Marie Sklodowska Curie Fellowship (reintegration)
- 2014-2015: New York Stem Cell Foundation-Druckenmiller Fellow.
- 2014: 1) ASH-EHA Translational Research Training in Hematology Program.
2) American Association of Immunologists New Investigator Travel Award.
- 2012-2014: Dana Fellow in Biomedical Research. Clinical Scholars Biomedical Research Training Program in Memorial Sloan-Kettering Cancer Center.
- 2009: 1) “Arkagathos Goutas” Award from the Greek Society of Hematology.
2) Best Oral Presentation Award. 20th Panhellenic Hematology Congress.
- 2008: Travel Award from American Society of Hematology.
- 2008: 1) Best Oral Presentation Award. 19th Panhellenic Hematology Congress.
2) Best Abstract Award. 19th Panhellenic Hematology Congress.
- 2008: 34th Annual Meeting of the European Group for Blood and Marrow Transplantation. Oral Presentation at the Presidential Symposium (5 best abstracts).
- 2007: Best Poster Award. 18th Panhellenic Hematology Congress.
- 2006-2007: The Greek State Scholarship Foundation Award. 1st among the graduates of Patras University Medical School.
- 2006: 1st Prize in the 1st Oncology Summer School for Medical Students.
- 2001-2002: “Koutsogeorgopoulos” award from the University of Patras Medical School being the best student in the course of Biochemistry.
- 2000-2003: The Greek State Scholarship Foundation Award. 1st among the candidates that entered Patras University Medical School and 1st among the students of 1st and 2nd year.

PROFESSIONAL MEMBERSHIPS

1. Member of the American Society of Hematology
2. Member of European Hematology Association
3. Member of the International Society for Stem Cell Research
4. Founding member of Patras University Medical School Graduates’ Association

RESEARCH FUNDING

1. Marie Sklodowska Curie Individual Fellowship, European Commission (165.598,80 Euro): “Generation of safe and efficient, off-the-shelf, chimeric antigen receptor (CAR)-engineered T cells for broad application” 2015-2017
2. Dutch Cancer Society Research grant (572.413 Euro) 2015-2019
3. Cancer Center Amsterdam Fellowship for junior group leader (341.000 euro).
4. Multiple Myeloma Research Foundation, Immunotherapy Network of excellence (800.000 Euro) 2018-2020

PATENTS

1. Effective generation of tumor-targeted T cells derived from pluripotent stem cells.
PCT/US2014/032883

INVITED SPEAKER

1. Combined CAR-T Congress Europe, Berlin, 30-31 January 2018. “Generation of off-the-shelf synthetic T cells in a dish for cancer immunotherapy”
2. 21st NAT Congress, Nantes 2016 “When Stem Cells meet Immunology”
3. Annual International Medical Students Meeting, Lisbon 7-9 March 2014. “A duet to boost cancer immunotherapy: Combining iPS and CARs”.

TEACHING

Lectures

1. Lectures for the Master Program “Stem cells and regenerative medicine” at the University of Patras Medical School.
2. Laboratory practical training in Hematology of 2nd year Medical students of VU (Vrije Universiteit) medical school.
3. Lectures in Oncology minor, 3rd year Medical students of VU (Vrije Universiteit) medical school.

Supervision graduate students, postdoctoral fellows and non-academic staff

1. Co-promotor, main daily supervisor of PhD candidate Afroditi Katsarou (2017-2021). Project: Development of “off-the-shelf”, spatio-temporally controllable Chimeric Antigen Receptor-engineered T lymphocytes for Multiple Myeloma therapy.
2. Co-promotor of PhD candidate Jia-Xian Wang (2017-2021). Project: Overcoming multiple myeloma-induced suppression of osteogenic differentiation.
3. Co-promotor of PhD candidate Jort van der Schans (2017-2021). Project: Dual CAR strategy for Multiple Myeloma and Acute Myeloid Leukemia.
4. Supervision of postdoctoral fellow Henk Jan Prins (2016-2019).
5. Supervisor of research technician Aida Farahani-Shahrabi (2016-2020).

OTHER NON-ACADEMIC ACTIVITIES

1. Consultancy for Covagen AG.

LANGUAGES

Greek: native

English: Professional proficiency (Certificate of Proficiency in English, Cambridge University)

Dutch: Working proficiency level NT2II/B2

French: Elementary proficiency (D.E.L.F. 1er Degre/A2, Institute Francaise)

German: Elementary proficiency (Goethe Institute Zertifikat/A2)

Spanish: Elementary proficiency

PUBLICATIONS in peer reviewed journals

1. Naik J, **Themeli M**, de Jong-Korlaar R, Ruiter RWJ, Poddighe PJ, Yuan H, de Bruijn JD, Ossenkoppele GJ, Zweegman S, Smit L, Mutis T, Martens ACM, van de Donk NWCJ, Groen RWJ. CD38 as a therapeutic target for adult acute myeloid leukemia and T-cell acute lymphoblastic leukemia. *Haematologica*. 2018 Sep 6.
2. Drent E, Poels R, Mulders MJ, van de Donk NWCJ, **Themeli M**, Lokhorst HM, Mutis T. Feasibility of controlling CD38-CAR T cell activity with a Tet-on inducible CAR design. *PLoS One*. 2018 May 30;13(5):e0197349.
3. Frerichs KA, Nagy NA, Lindenbergh PL, Bosman P, Marin Soto J, Broekmans M, Groen RWJ, **Themeli M**, Nieuwenhuis L, Stege C, Nijhof IS, Mutis T, Zweegman S, Lokhorst HM, van de Donk NWCJ. CD38-targeting antibodies in multiple myeloma: mechanisms of action and clinical experience. *Expert Rev Clin Immunol*. 2018 Mar;14(3):197-206.
4. Drent E, **Themeli M**, Poels R, de Jong-Korlaar R, Yuan H, de Bruijn J, Martens ACM, Zweegman S, van de Donk NWCJ, Groen RWJ, Lokhorst HM, Mutis T. A Rational Strategy for Reducing On-Target Off-Tumor Effects of CD38-Chimeric Antigen Receptors by Affinity Optimization. *Mol Ther*. 2017 Aug 2;25(8):1946-1958.
5. Drent E, Groen RW, Noort WA, **Themeli M**, Lammerts van Bueren JJ, Parren PW, Kuball J, Sebestyen Z, Yuan H, de Bruijn J, van de Donk NW, Martens AC, Lokhorst HM, Mutis T. Preclinical evaluation of CD38 chimeric antigen receptor engineered T cells for the treatment of multiple myeloma. *Haematologica*. 2016 Feb 8;101(5):616-25
6. **Themeli M**, Sadelain M. Combinatorial Antigen Targeting: Ideal T-Cell Sensing and Anti-Tumor Response. *Trends Mol Med*. 2016 Mar 10.
7. Kotini AG, de Stanchina E, **Themeli M**, Sadelain M, Papapetrou EP. Escape Mutations, Ganciclovir Resistance, and Teratoma Formation in Human iPSCs Expressing an HSVtk Suicide Gene. *Mol Ther Nucleic Acids*. 2016 Feb 2;5:e284
8. **Themeli M**, Rivière I, Sadelain M. New cell sources for T cell engineering and adoptive immunotherapy. *Cell Stem Cell*. 2015 Apr 2;16(4):357-66.
9. Perna F, Vu LP, **Themeli M**, Kriks S, Hoya-Arias R, Khanin R, Hricik T, Mansilla-Soto J, Papapetrou EP, Levine RL, Studer L, Sadelain M, Nimer SD. The Polycomb Group Protein L3MBTL1 Represses a SMAD5-Mediated Hematopoietic Transcriptional Program in Human Pluripotent Stem Cells. *Stem Cell Reports*. 2015 Apr 14;4(4):658-69
10. Fedorov V.D., **Themeli M.**, Sadelain M. PD-1- and CTLA-4-based inhibitory chimeric antigen receptors (iCARs) divert off-target immunotherapy responses. *Sci Transl Med*. 2013 Dec 11;5(215):215ra172.
11. **Themeli M**, Kloss CC, Ciriello G, Fedorov VD, Perna F, Gonen M, Sadelain M. Generation of tumor-targeted human T lymphocytes from induced pluripotent stem cells for cancer therapy. *Nat Biotechnol*. 2013 Oct;31(10):928-33.
12. **Themeli M**, Spyridonidis A. DNA damage and repair in epithelium after allogeneic hematopoietic stem cell transplantation. *Int J Mol Sci*. 2012 Nov 27;13(12):15813-25. doi: 10.3390/ijms131215813.
13. Lazana I, Zoudiari A, Kokkinou D, **Themeli M**, Liga M, Papadaki H, Papachristou D, Spyridonidis A. Identification of a novel HLA-G+ regulatory population in blood: expansion after allogeneic transplantation and de novo HLA-G expression at graft-versus-host disease sites. *Haematologica*. 2012 Sep;97(9):1338-47. doi:

- 10.3324/haematol.2011.055871.
14. **Themeli M**, Waterhouse M, Finke J, Spyridonidis A. DNA chimerism and its consequences after allogeneic hematopoietic cell transplantation. *Chimerism*. 2011 Jan;2(1):25-28.
 15. Spyridonidis A, Liga M, Triantafyllou E, **Themeli M**, Marangos M, Karakantza M, Zoumbos N. Pharmacokinetics and clinical activity of very low-dose alemtuzumab in transplantation for acute leukemia. *Bone Marrow Transplant*. 2011 Oct;46(10):1363-8. doi: 10.1038/bmt.2010.308.
 16. Waterhouse M, **Themeli M**, Bertz H, Zoumbos N, Finke J, Spyridonidis A. Horizontal DNA transfer from donor to host cells as an alternative mechanism of epithelial chimerism after allogeneic hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2011 Mar;17(3):319-29. doi: 10.1016/j.bbmt.2010.09.001.
 17. **Themeli M**, Petrikos L, Waterhouse M, Bertz H, Lagadinou E, Zoumbos N, Finke J, Spyridonidis A. Alloreactive microenvironment after human hematopoietic cell transplantation induces genomic alterations in epithelium through an ROS-mediated mechanism: in vivo and in vitro study and implications to secondary neoplasia. *Leukemia*. 2010 Mar;24(3):536-43. doi: 10.1038/leu.2009.284.
 18. Waterhouse M, **Themeli M**, Metaxas Y, Lagadinou ED, Finke J, Spyridonidis A. Horizontal DNA and mRNA transfer between donor and recipient cells after allogeneic hematopoietic cell transplantation? *Front Biosci (Landmark Ed)*. 2009 Jan 1;14:2704-13. Review.

TEXTBOOK CHAPTERS

1. Spyridonidis A., Metaxas Y., Themeli M., Bertz H., Zoumbos N., Finke J. New insights in the development of biological chimeras: Genomic Instability and Epithelial Chimerism after HSCT. In **Hematopoietic Stem Cell Transplantation Research Advances** (Ed. F. Columbus) Nova Science Publishers, Inc.
2. Themeli M, Waterhouse M, Metaxas Y, Lagadinou E, Zoumbos N, Finke J, Spyridonidis A. Epithelial chimerism and genomic instability after allogeneic HCT: two aspects of the same phenomenon. In **New Insights in Hematopoietic Cell Transplantation** (Ed. A. Spyridonidis and I. Sakellari) Research Signpost.

SELECTED ABSTRACTS PRESENTED IN SCIENTIFIC MEETINGS (abstracts selected for oral announcement):

1. **Maria Themeli** and Michel Sadelain. Chimeric-antigen receptor engineered human T lymphocytes from induced pluripotent stem cells for cancer therapy. American Association of Immunologists Annual Meeting, May 2-6 2014, Pittsburgh.
2. Fedorov VD, **Themeli M**, Sadelain M. iCARs: Novel Engineered Cell-Intrinsic Safety Switches For Prevention of Immunotherapy Toxicities. Keystone Symposia on Engineering Cell Fate and Function, Apr 6 - Apr 11, 2014, Resort at Squaw Creek in Olympic Valley, CA.
3. **Themeli M**, Kloss CC, Ciriello G, Fedorov VD, Perna F, Gonen M, Sadelain M. Generation of tumor-targeted human T lymphocytes from induced pluripotent stem cells for cancer therapy. Generation of functional tumor-targeted T lymphocytes from

human chimeric antigen receptor-engineered induced pluripotent stem cells. ISEH 42nd Annual Scientific Meeting, Vienna 22-25 August 2013.

1. **Maria Themeli**, Christopher C. Kloss, Michel Sadelain. Human iPS-derived antigen-targeted T cells eradicate CD19-positive tumor cells. Human iPS cell-derived antigen-targeted T lymphocytes eradicate CD19-positive tumor cells. ISSCR Annual Meeting, Boston 12-15 June 2013.
2. **Maria Themeli**, Christopher C. Kloss, Michel Sadelain. Human iPS-derived antigen-targeted T cells eradicate CD19-positive tumor cells. NYSTEM Annual Meeting: Collaboration and renewal, New York 23-23 May 2013.
3. **Maria Themeli**, Christopher C. Kloss, Giovanni Ciriello, Michel Sadelain. Human iPS-derived antigen-targeted T cells are functional innate-like cytotoxic effectors and lyse CD19-positive tumor cells. American Society of Gene and Cell Therapy Annual Meeting, Salt Lake City 15-18 May 2013.
4. Fabiana Perna, Ly P. Vu, **Maria Themeli**, Ruben Hoya-Arias, Xinyang Zhao, Eirini P. Papapetrou, Michel Sadelain and Stephen D. Nimer. Targeting a novel epigenetic silencing mechanism to efficiently upregulate fetal globin gene expression. American Society of Hematology Annual Meeting, San Diego 10-13 December 2011.
5. Lagadinou E, Kokkinou D, **Themeli M**, Dimas K, Spyridonidis A, Zoumbos N. A ROS^{low} redox state characterizes a distinct subpopulation of leukemic blasts with stem cell properties in acute myeloid leukemia. 20th Panhellenic Hematology Congress. Heraklion 4-7 November 2009. **Best oral presentation award.**
6. Lazana I, **Themeli M**, Zoudiari A, Kokkinou D, Lagadinou E, Zoumbos N, Spyridonidis A. Detection and isolation of naturally occurring HLA-G positive cells with immunoregulatory function in peripheral blood of healthy donors. 20th Panhellenic Hematology Congress. Heraklion 4-7 November 2009. **Best oral presentation award.**
7. **Themeli M**, Petrikkos L, Waterhouse M, Bertz H, Zoumbos N, Finke J, Spyridonidis A. Alloantigenic reactions after human hematopoietic cell transplantation induce genomic alterations in epithelium: a confirmation in vivo and in vitro study and implications to secondary neoplasia. American Society of Hematology Annual Meeting, San Francisco 4-9 December 2008. **Travel Award.**
8. Lagadinou E, Kokkinou D, **Themeli M**, Dimas K, Spyridonidis A, Zoumbos N. Characterization of distinct leukemic subsets according to their redox status. 19th Panhellenic Hematology Congress. Athens 16-22 November 2008. **Best abstract award.**
9. **Themeli M**, Lagadinou E, Zoudiari N, Klamargias A, Kokkinou D, Zoumbos N, Spyridonidis A. Alloantigenic reactions after human hematopoietic cell transplantation induce genomic alterations in epithelium: a confirmation in vivo and in vitro study and implications to secondary neoplasia. 19th Panhellenic Hematology Congress. Athens 16-22 November 2008. **Best Oral Presentation.**
10. **Themeli M**, Petrikkos L, Waterhouse M, Bertz H, Zoumbos N, Finke J, Spyridonidis A. Alloantigenic reactions after human hematopoietic cell transplantation induce genomic alterations in epithelium: a confirmation in vivo and in vitro study and implications to secondary neoplasia. 34th Annual Meeting of the European Group for Blood and Marrow Transplantation. Florence March 30-April 2 2008. **Oral presentation at the Presidential Symposium among 5 best abstracts.**