PERSONAL INFORMATION

Michele Milella

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Sex M | Date of birth 01/03/1968 | Nationality Italian

Current Position: Full Professor of Oncology (SC 06/D3 - SSD MED06 - Oncologia Medica), Section Head, University of Verona - School of Medicine, Department of Medicine

PhD awarded less than 10 Years ago: No

GOLDEN PARAGRAPH

Scientific Profile: I am an experienced Medical Oncologist with a sincere passion for translational research. Since my beginnings in Medical School, I have been fascinated by the possibility that medicine could indeed become a "science", as much based on personal experience as on a deep understanding of the molecular and biological mechanisms underlying pathological processes and the action of drugs and therapeutic procedures. For this very reason, I followed the training path of a so-called "physician/scientist" over my entire career. I trained in Immunology (tumor immunology, molecular mechanisms of signal transduction regulating NK cell activation) and Medical Oncology (anti-emetic treatment, H/N, breast, lung, and bladder cancer, design and conduction of clinical trials, application of gene transduction techniques to the immunotherapy of bladder cancer, and biostatistical methodology). I subsequently enrolled in a postdoctoral fellowship in molecular hematology at the M. D. Anderson Cancer Center in Houston, where I was exposed to the fascination of probabilistic Bayesian approaches to statistical reasoning and started the line of research that has characterized my preclinical/translational activity to these days: targeting signaling intermediates (essentially the MAPK and PI3K/mTOR pathways) for therapeutic purposes in leukemias and solid tumors. Back to clinical oncology I developed a pancreatic cancer program at the Regina Elena National Cancer Institute and became responsible for the clinical management and research programs on hepato-bilio-pancreatic cancers, thoracic cancers, NET (including rarer forms such as Merkel cell carcinoma), and kidney cancer. Most recently, I contributed to the building of an AIFA certified Phase I/early phase clinical trial centre, in which I served as Medical Director.
In my new role as full professor of Oncology and director of Oncology at the University of Verona/AOUI Verona, my main objective has been to develop a new model of cancer medicine, whereby patient management and treatment decisions are guided by a profound knowledge of disease biology in individual patients. Molecular pathology, a keen attitude of the group to work in a multidisciplinary setting, and the translational tradition of my current environment, all concur to make the realization of an effective precision oncology program within reach at our Institution, giving us the possibility to change our clinical practice into a personalized, precise and humane "cancer science" centered on each individual patient.
Clinical research activity has been characterized by an interest in developing novel targeted therapy approaches, identifying and validating prognostic and predictive biomarkers, and developing meta-analytical approaches to evidence-based oncology, with special focus on: ***pancreatic and hepato-biliary*** cancers, ***lung*** cancer, ***kidney*** cancer, and ***neuroendocrine*** tumors. At the same time, I led a preclinical and translational group, whose research focus has been on the development new targeted drugs, particularly MAPK and PI3K/mTOR inhibitors, development of combinations of targeted drugs exploiting synergistic antitumor interactions, identification and validation of biomarkers of sensitivity/resistance to targeted treatments (with a focus on the potential role of PTEN), and most recently microenvironmental interactions between tumor and stromal cells.

Preclinical/Translational Research:

1. Tumor immunology, with a focus on molecular mechanisms of signal transduction regulating NK cell activation through the engagement of Fc receptors and integrins
2. Gene transduction-based immunotherapy of bladder cancer, using engineered tumor cells producing IL-2
3. Targeting signaling intermediates (MAPK and PI3K/mTOR pathways) for therapeutic purposes in leukemias and solid tumors
4. Tumor/microenvironment interactions in the regulation of sensitivity/resistance to molecularly targeted anticancer therapy
5. Molecular mechanisms of regulation of pro-inflammatory cytokines production by tumor cells and tumor microenvironment (with a special focus on IL-8 regulation)
6. Genomic profiling and circulating biomarkers monitoring to assess sensitivity/resistance to immunotherapy
7. Alternative therapeutic targeting strategies (e.g. inducing exon skipping) for currently undruggable molecular drivers

Clinical Research:

1. PI or Co-I in >150 clinical trials, including Phase I and First-in-Human studies, exploring novel therapeutic approaches in breast, H/N, hepato-bilio-pancreatic, thoracic, genitourinary cancers and NET (including rarer forms such as Merkel cell carcinoma)
2. Development of novel molecularly targeted therapy approaches in solid tumors
3. Identification and validation of novel prognostic and predictive biomarkers
4. Development of meta-analytical approaches to evidence-based oncology
5. Development of Precision Oncology programs based on broad genomic profiling and Molecular Tumor Board-based therapeutic recommendations
6. Supportive care in cancer patients, with a special focus on the prevention and treatment of chemotherapy-induced emesis
7. Integrated approach to early supportive care in cancer patients, encompassing nutritional, physical exercise, and psychological intervention, with a focus on identification of molecular correlates of such intervention (FOcus on Research and CarE - FORCE project)

Bibliometric Indicators:

Publications: 334; # Citations 18320; H index 55;

3 most relevant publications or patents:

1. ICGC-ARGO precision medicine: familial matters in pancreatic cancer. Milella M, Luchini C, Lawlor RT, Johns AL, Casolino R, Yoshino T, Biankin AV; ICGC-ARGO.Lancet Oncol. 2022 Jan;23(1):25-26. doi: 10.1016/S1470-2045(21)00703-8.PMID: 34973218 No abstract available.
2. Molecular Tumor Boards in Clinical Practice. Luchini C, Lawlor RT, Milella M, Scarpa A.Trends Cancer. 2020 Sep;6(9):738-744. doi: 10.1016/j.trecan.2020.05.008. Epub 2020 Jun 6.PMID: 32517959
3. Pan-cancer analysis of whole genomes. ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium.Nature. 2020 Feb;578(7793):82-93. doi: 10.1038/s41586-020-1969-6. Epub 2020 Feb 5.PMID: 32025007

ROLE IN THE PROJECT

Clinical/translational research (Spoke 8) aimed at implementing: 1) novel targeted therapeutic approaches in advanced pancreatic cancer; 2) lifestyle interventions aimed at modifying immune responsiveness in lung and breast cancers; 3) NGS-based broad molecular profiling and MTB-based selection of therpautic options in rare and orphan tumors (PONTE).

WORK EXPERIENCE

2020-current: Member of the Board of Administrators, Centro Ricerche Cliniche di Verona.
Main duties/responsibilities: Business development and operations management
Sector: Clinical Trials, including Phase I and First-In-Human CT, as well as CT in Healthy Volunteers'

2020-current: Special Commissioner to the COVID19 logistics, Verona University and Hospital Trust (AOUI Verona)
Main duties/responsibilities: Coordination of the hospital's COVID-19 response task force
Sector: Covid-19 emergency management, Public Health

2020-current: Member of the Ethical Committee for Clinical Research of the Verona and Rovigo provinces.
Main duties/responsibilities: Evaluation and authorization of interventional and observational Clinical Trials; evaluation and authorization of named patient program/compassionate use drug requests for individual patients
Sector: Ethical Committee for Clinical Research

2018-current: Full Professor of Oncology, Section Head, University of Verona - School of Medicine, Department of Medicine
Main duties/responsibilities: Teaching activity in Oncology (MD and other courses, Specialty schools); coordination and management of the research activity of the Section
Sector: Education, Health

2018-current: Director, UOC Oncology**,** AOUI Verona.
Main duties/responsibilities: Coordination and management of the Oncology Division of the AOUI Verona (Policinico G. B. Rossi and Ospedale Civile Maggiore)
Sector: Health

2018-current: Director, Residency Program in Medical Oncology**,** University of Verona - School of Medicine
Main duties/responsibilities: Coordination of the School's training activities; individual student's tutoring
Sector: Education

2017-2018: Medical Director, Centro Studi Early Phase (CSEP), IRCCS Regina Elena National Cancer Institute, Rome.
Main duties/responsibilities: Phase I and early phase II clinical trials; coordination, management and certification maintenance of the Phase I CT unit
Sector: Clinical Trials, including Phase I and First-In-Human CT

2001-2018: Senior staff member, Attending physician, Medical Oncology 1, IRCCS Regina Elena National Cancer Institute, Rome
Main duties/responsibilities: Coordination of clinical and research activities; coordination of the preclinical and translational research lab of the Medical Oncology 1 Division
Sector: Health

EDUCATION AND TRAINING

1999-2002: Postdoctoral fellowship. University of Texas M. D. Anderson Cancer Center, Houston, TX Section of Molecular Hematology and Therapy, Dept. of Blood and Marrow Transplantation (preclinical and translational signal transduction targeting as a therapeutic strategy in cancer)

1992-1996: Residency and National Board Certification in Medical Oncology. University of Rome "La Sapienza"

1986-1992: Medical School and MD degree in Medicine and Surgery. University of Rome "La Sapienza"

PERSONAL SKILLS

Organisational / managerial skills

Currently coordinator of a team of 14 staff physicians, 3 PhD students, 44 Medical Oncology fellows, and 1 biologist.
Team leader in several preclinical, translational, and clinical research projects from 2002 to date.
Member of the Board of Directors and Scientific committees of the Italian Association for the Study of Pancreas (**AISP**, since 2016), Italian Foundation for Pancreatic Diseases (**FIMP**, since 2014), AIOM guidelines on Diagnosis and Treatment of Pancreatic Cancer (since 2016). Regional Secretary of the AIOM Section Regione Lazio (2009-2011).

ADDITIONAL INFORMATION

Selected pubs 2021-22

1. Non-functional pancreatic neuroendocrine tumours: ATRX/DAXX and alternative lengthening of telomeres (ALT) are prognostically independent from ARX/PDX1 expression and tumour size. Hackeng WM, et al.Gut. 2022 May;71(5):961-973. doi: 10.1136/gutjnl-2020-322595.
2. SEMA6A/RhoA/YAP axis mediates tumor-stroma interactions and prevents response to dual BRAF/MEK inhibition in BRAF-mutant melanoma. Loria R, et al. J Exp Clin Cancer Res. 2022 Apr 19;41(1):148. doi: 10.1186/s13046-022-02354-w.
3. Risk and severity of SARS-CoV-2 infection in breast cancer patients undergoing a structured infection screening program at the University and Hospital Trust of Verona. Zanelli S, et al. Ann Oncol. 2022 Mar 9:S0923-7534(22)00363-5. doi: 10.1016/j.annonc.2022.02.227.
4. Nutritional support in lung cancer: Time to combine immunonutrition with immunotherapy? Pilotto S, et al. Nutrition. 2022 Mar 3;98:111637. doi: 10.1016/j.nut.2022.111637.
5. Integrative molecular analysis of combined small-cell lung carcinomas identifies major subtypes with different therapeutic opportunities. Simbolo M, et al. ESMO Open. 2022 Feb;7(1):100308. doi: 10.1016/j.esmoop.2021.100308.
6. ICGC-ARGO precision medicine: familial matters in pancreatic cancer. Milella M, et al. Lancet Oncol. 2022 Jan;23(1):25-26. doi: 10.1016/S1470-2045(21)00703-8.
7. Evolving pancreatic cancer treatment: From diagnosis to healthcare management. Milella M, et al. Crit Rev Oncol Hematol. 2022 Jan;169:103571. doi: 10.1016/j.critrevonc.2021.103571.
8. Genomic characterization of hepatoid tumors: context matters. Lawlor RT, et al. Hum Pathol. 2021 Dec;118:30-41. doi: 10.1016/j.humpath.2021.09.006.
9. Impact of COVID-19 on Pancreatic Cancer Research and the Path Forward. Casolino R, et al. .Gastroenterology. 2021 Dec;161(6):1758-1763. doi: 10.1053/j.gastro.2021.06.080.
10. Chemotherapy toxicity and activity in patients with pancreatic ductal adenocarcinoma and germline BRCA1-2 pathogenic variants (gBRCA1-2pv): a multicenter survey. Orsi G, et al. ESMO Open. 2021 Oct;6(5):100238. doi: 10.1016/j.esmoop.2021.100238.
11. Immune landscape, evolution, hypoxia-mediated viral mimicry pathways and therapeutic potential in molecular subtypes of pancreatic neuroendocrine tumours. Young K, et al. Gut. 2021 Oct;70(10):1904-1913. doi: 10.1136/gutjnl-2020-321016.
12. Neoadjuvant treatment: A window of opportunity for nutritional prehabilitation in patients with pancreatic ductal adenocarcinoma. Trestini I, et al. World J Gastrointest Surg. 2021 Sep 27;13(9):885-903. doi: 10.4240/wjgs.v13.i9.885.
13. Pancreatic Enzyme Replacement Therapy in Patients Undergoing First-Line Gemcitabine Plus *nab*-paclitaxel for Advanced Pancreatic Adenocarcinoma. Trestini I, et al. Front Oncol. 2021 Sep 9;11:688889. doi: 10.3389/fonc.2021.688889. eCollection 2021.
14. Adjuvant Pembrolizumab after Nephrectomy in Renal-Cell Carcinoma. Choueiri TK, et al. N Engl J Med. 2021 Aug 19;385(8):683-694. doi: 10.1056/NEJMoa2106391.PMID: 34407342
15. Homologous Recombination Deficiency in Pancreatic Cancer: A Systematic Review and Prevalence Meta-Analysis. Casolino R, et al. J Clin Oncol. 2021 Aug

10;39(23):2617-2631. doi: 10.1200/JCO.20.03238.
16. A multimodal approach to cancer-related cachexia: from theory to practice. Avancini A, Expert Rev Anticancer Ther. 2021 Aug;21(8):819-826. doi: 10.1080/14737140.2021.1927720.
17. A narrative review on tumor microenvironment in oligometastatic and oligoprogressive non-small cell lung cancer: a lot remains to be done. Belluomini L, et al. Transl Lung Cancer Res. 2021 Jul;10(7):3369-3384. doi: 10.21037/tlcr-20-1134.

Projects/Grants

Principal Investigator/Group Leader

2002-2005: Functional and molecular characterization of the effects of therapeutic agents interfering with signal transduction and transcription (MoH)
2004-2007: Preclinical development of MEK inhibition-based therapeutic strategies for acute leukemias (AIRC)
2008-2010: Therapeutic MEK targeting in preclinical models of hematologic malignancies and solid tumors (AIRC)
2010-2012: Integrating novel clinical and biomolecular prognostic/predictive factors for risk stratification and treatment assignment: the silent revolution of Non-Small Cell Lung Cancer (NSCLC) (MoH)
2011-2015: Development of effective cancer therapies based on functional proteomics and cancer stem cell targeting (AIRC - Special Program Molecular Clinical Oncology 5 per mille)
2013-2016: KRAS mutations and DNA repair function in NSCLC - Bio-RARE (MoH - ERANET/TRANSCAN)
2014-2016: Beyond single pathway inhibition: MEK inhibition-based "vertical" and "lateral" combinations (AIRC)
2015: FOLFIRINOX optimization for the routine management of pancreatic cancer patients: clinical impact of dose/schedule modifications and potential for pharmacogenomics-based strategies for patient selection and treatment personalization (MoH - Institutional Current Research funding)
2016-2017: Development of effective cancer therapies based on functional proteomics and cancer stem cell targeting (AIRC - Special Program Molecular Clinical Oncology 5 per mille/Multiunit extension)
2016-2018: Beyond tumor cell targeting with pathway inhibitors in human melanoma: role of the microenvironment (AIRC)
2019-2021: Applicative translation of the results of genomic research on pancreatic cancer (MoH - FIMP)
2022-2025: Gene/environment interactions in breast and thyroid cancers: defining the biological role of and actioning endocrine disruptors (ED) and lifestyle to develop rational therapeutic/preventive interventions. ASTEROID- breASt Thyroid cancERs endOcrIne Disruptors (Funding agency: MUR)

Honours and awards

AIRC fellowship for Oncological Research (**1992**)
Degree's Thesis Award "Pasteur Institute - Cenci Bolognetti Foundation" (**1994**)
American Cancer Society International Fellowship for Beginning Investigators (ACSBI administered by UICC (**1999/2000**)
Award of the National Committee for Biomedical Sciences (Italian National Research Counc – CNR) (**1999**)

According to law 679/2016 of the Regulation of the European Parliament of 27th April 2016, I hereby express my consent to process and use my data provided in this CV

Verona, February 4th, 2025 *Michele Milella*