Curriculum vitae
Carla Boccaccio

Personal details

Born in: Genova, October 22, 1966

Nationality: Italian

Email: carla.boccaccio@unito.it; carla.boccaccio@ircc.it

Website: https://www.irccs.org/cancer-stem-cell-research

ORCID ID: 0000-0003-2620-9083; Scopus ID: 56247814200; Researcher ID: AHE-7875-2022

Education

October 1996: Board Certificate in Clinical Pathology, University of Turin School of Medicine (Turin, Italy) – summa cum laude.

July 1991: Degree in Medicine and Surgery, University of Turin School of Medicine (Turin, Italy) – summa cum laude.

Current position and professional experiences

Current position

October 2001-present: Associate Professor of Histology, Department of Oncology, University of Turin (Turin, Italy).

January 2006-present: Group Leader, Laboratory of Cancer Stem Cell Research, Candiolo Cancer Institute, FPO-IRCCS (Candiolo, Turin).

Professional experiences

September 1995 - September 2001: Assistant Professor of Histology, Department of Biomedical Sciences and Human Oncology, University of Turin.

June 1996 - December 2005: Researcher, Division of Molecular Oncology, IRCC (Candiolo, Turin) (Director: Prof. P.M. Comoglio).

July 1991 - September 1995: Post-doc, Department of Biomedical Sciences and Human Oncology, University of Turin (Supervisor: Prof. P.M. Comoglio).

Honors

2005: Highly Commended Young Cancer Researcher Award, European Association for Cancer Research.

Teaching activity

2001-present - Associate Professor - Histology and Embryology - Course in Medicine and Surgery - University of Turin (Turin, Italy)

1995-2001 - Research Assistant - Histology and Embryology - Course in Medicine and Surgery - University of Turin (Turin, Italy)

2008-present - Teacher and Supervisor - PhD Program in Molecular Medicine (Cell Sciences and Technology) - University of Turin (Turin, Italy)

2001-2007- Teacher and Supervisor - PhD Program in Cell Sciences and Technology - Medical School - University of Turin (Turin, Italy)

2018-present - Teacher and Supervisor - Cancer stem cells as therapeutic targets - MD/PhD Course, School of Medicine - University of Turin (Turin, Italy)

2019-present - Teacher and Supervisor - Laboratory course on Cancer Stem Cells - Course in Medical Biotechnology - University of Turin (Turin, Italy).

Research main topics

- Characterization of cancer stem cells in glioblastoma and metastatic tumors, specifically colorectal and lung cancer, and cancer of unknown primary origin. This involves a focus on the interplay between genetic landscape, transcriptional profile, cell signaling and regulation, and response to therapeutic agents.
- Development of deeply characterized preclinical platforms including *in vitro* 3D models and *in vivo* tumors generated by cancer stem cells. This aims for the preclinical assessment of experimental therapies, with a focus on receptor tyrosine kinase inhibitors and combination treatments.

Main projects as PI

As an independent investigator (PI of the Cancer Stem Cell Research Lab, Candiolo Cancer Institute), Carla Boccaccio continued to explore the role of the MET oncogene (HGF receptor) in human cancer, building upon studies carried out in her early career. She recontextualized MET, known as a driver of cancer epithelial-mesenchymal transition and invasive growth, trying to understand how this receptor impinges on the core properties of cancer stem cells - the cells considered responsible for tumor generation and dissemination, clonal evolution, and ultimately therapeutic resistance (Nat. Rev. Cancer, 6:637, 2006). This interest prompted her to delve deeper into the global molecular and genetic profile of cancer stem cells. Concurrently, she capitalized on extensive panels of patient-derived, clinically annotated cancer stem cells to construct well-characterized and integrated preclinical platforms, including 3D *in vitro* models (tumor spheres and organoids), patient-derived xenografts, and mouse models generated by tumor sphere transplantation (spheropatients).

- *MET in glioblastoma stem cells*. Carla Boccaccio and her team discovered that MET supports therapeutic resistance of cancer stem cells from glioblastomas and other tumors. Their research pinpointed the mechanism behind MET induction by genotoxic damage, involving the NF-kB pathway, leading to an invasive and radioresistant phenotype (J. Natl. Cancer Inst. 103:645, 2011). Subsequently, they showed that MET serves as a functional marker of a glioblastoma stem cell subtype, which can be sensitized to irradiation by MET inhibitors (Cancer Res.,

72:4537, 2012; EMBO Mol. Med., 8:550, 2016). These studies not only showcased that MET-targeted therapy enhances radiotherapy efficacy (patent EP2500036B1) but also highlighted the role of Carla Boccaccio in establishing and coordinating a collaborative network of cell biologists, geneticists, clinicians and bioinformaticians. This network supported the generation and full characterization of an integrated preclinical platform including >150 glioblastoma stem cell 3D-cultures (neurospheres), matched tissues from clinically-annotated primary and recurrent glioblastomas, and related patient-derived xenografts and spheropatients.

- *Glioblastoma stem cell heterogeneity*. This platform lead to discover that the ERBB3 oncogene is a candidate therapeutic target in a glioblastoma subset (Cell Rep., 36:109455, 2021), and to show that cancer stem cells with different genetic and transcriptional features coexist in individual glioblastomas. This finding contributed to our understanding of glioblastoma heterogeneity and the factors underlying therapeutic failure (Cell Rep., 42:112816, 2023). These studies laid the foundation for ongoing research aimed at comprehensively deciphering the molecular mechanisms of therapeutic resistance operating in glioblastoma stem cells.
- *Glioblastoma liquid biopsy*. Leveraging their knowledge of glioblastoma genetics, Carla Boccaccio and her team, supported by a clinical network, provided insights into performing liquid biopsy of cerebrospinal fluid for the diagnosis of first-presentation gliomas (Clin. Can. Res., 29:1252, 2023; Critical Rev. Oncol. Hemat., 9:1546, 2020).
- *Metastatic colorectal cancer: MET and more*. Considering MET functions in the stem compartment of gut epithelia and its ability to promote invasive growth – a property underlying metastasis, which Carla Boccaccio explored in her earlier studies – her team characterized cancer stem cells isolated from metastatic colorectal cancer. By integrating an extensive platform of *in vitro* and *in vivo* models (colospheres and spheropatients), they dissected the role of MET and EGFR family as therapeutic targets and drivers of invasion (Cancer Res., 74:1857, 2014; 74:3647, 2014; Clin. Can. Res., 24:807, 2018; Mol Oncol., 17:1280, 2023) and contributed to large cooperative studies investigating colorectal cancer metastasis (Nat Comm., 8:15107, 2017; Sci. Transl. Med., 12:eaax8313, 2020).
- *CUP: coupling cancer stemness and metastasis*. Carla Boccaccio has been coordinating a multi-disciplinary project exploring a lethal and still obscure malignancy defined as ‘cancer of unknown primary origin’ (CUP), which represents a paradigm of cancer metastasis. This effort revealed a tight relationship between the stem and the metastatic phenotype and lead to generation of the first preclinical CUP model, revealing vulnerability to inhibition of the MEK/MYC axis (Nat. Comm., 12:2498, 2021; EMBO Mol. Med., 15:e16104, 2023; EMBO Mol. Med., 12:e11756, 2020). The study of CUP pathogenetic mechanisms and therapeutic liability is currently ongoing.
- *MET genetic alterations and targeting*. Drawing on her long-standing experience, Carla Boccaccio continues to collaborate to studies exploring the role of MET in human cancer. Specifically, her focus is on MET genetic alterations as a promising therapeutic targeting in lung and other carcinomas (Nat. Rev. Cancer, 18:341, 2018).
- *Funding*. Carla Boccaccio’s projects have been supported by the Italian Association for Cancer Research (AIRC), Fondazione Piemontese per la Ricerca sul Cancro (FPRC), Italian Ministry of Health (PNRR, Next Generation EU), Italian Ministry of University and Research, European Union.

Bibliometry

h-index: 35

10 Best publications

1. De Bacco F, Orzan F, Crisafulli G, Prelli M, Isella C, Casanova E, Albano R, Reato G, Erriquez J, D'Ambrosio A, Panero M, Dall'Aglio C, Casorzo L, Cominelli M, Pagani F, Melcarne A, Zeppa P, Altieri R, Morra I, Cassoni P, Garbossa D, Cassisa A, Bartolini A, Pellegatta S, Comoglio PM, Finocchiaro G, Poliani PL, and Boccaccio C. (2023). Coexisting cancer stem cells with heterogeneous gene amplifications, transcriptional profiles, and malignancy are isolated from single glioblastomas. Cell Reports 42(8):112816. DOI: 10.1016/j.celrep.2023.112816. PMID: 37505981.

2. Orzan F, De Bacco F, Lazzarini E, Crisafulli G, Gasparini A, Dipasquale A, Barault L, Macagno M, Persico P, Pessina F, Bono B, Giordano L, Zeppa P, Melcarne A, Cassoni P, Garbossa D, Santoro A, Comoglio PM, Indraccolo S, Simonelli M, and Boccaccio C. (2023). Liquid Biopsy of Cerebrospinal Fluid Enables Selective Profiling of Glioma Molecular Subtypes at First Clinical Presentation. Clinical Cancer Research 29(7):1252-1266. DOI: 10.1158/1078-0432.CCR-22-2903. PMID: 36648487.

3. Verginelli F, Pisacane A, Gambardella G, D'Ambrosio A, Candiello E, Ferrio M, Panero M, Casorzo L, Benvenuti S, Cascardi E, Senetta R, Geuna E, Ballabio A, Montemurro F, Sapino A, Comoglio PM, and Boccaccio C. (2021). Cancer of unknown primary stem-like cells model multi-organ metastasis and unveil liability to MEK inhibition. Nature Communications 12(1):2498. DOI: 10.1038/s41467-021-22643-w. PMID: 33941777.

4. Comoglio PM, Trusolino L, and Boccaccio C. (2018). Known and novel roles of the MET oncogene in cancer: a coherent approach to targeted therapy. Nature Reviews Cancer 18(6):341-358. DOI: 10.1038/s41568-018-0002-y. PMID: 29674709.

5. De Bacco F, D'Ambrosio A, Casanova E, Orzan F, Neggia R, Albano R, Verginelli F, Cominelli M, Poliani PL, Luraghi P, Reato G, Pellegatta S, Finocchiaro G, Perera T, Garibaldi E, Gabriele P, Comoglio PM, and Boccaccio C. (2016). MET inhibition overcomes radiation resistance of glioblastoma stem-like cells. EMBO Molecular Medicine 8(5):550-68. DOI: 10.15252/emmm.201505890. PMID: 27138567.

6. Luraghi P, Reato G, Cipriano E, Sassi F, Orzan F, Bigatto V, De Bacco F, Menietti E, Han M, Rideout WM 3rd, Perera T, Bertotti A, Trusolino L, Comoglio PM, and Boccaccio C. (2014). MET signaling in colon cancer stem-like cells blunts the therapeutic response to EGFR inhibitors. Cancer Research 74(6):1857-69. DOI: 10.1158/0008-5472.CAN-13-2340-T. PMID: 24448239.

7. De Bacco F, Luraghi P, Medico E, Reato G, Girolami F, Perera T, Gabriele P, Comoglio PM, and Boccaccio C. (2011). Induction of MET by ionizing radiation and its role in radioresistance and invasive growth of cancer. Journal of the National Cancer Institute 103(8):645-61. DOI: 10.1093/jnci/djr093. PMID: 21464397.

8. Boccaccio C and Comoglio PM. (2006). Invasive growth: a MET-driven genetic programme for cancer and stem cells. Nature Reviews Cancer 6(8):637-45. DOI: 10.1038/nrc1912. PMID: 16862193.

9. Boccaccio C, Sabatino G, Medico E, Girolami F, Follenzi A, Reato G, Sottile A, Naldini L, and Comoglio PM. (2005). The MET oncogene drives a genetic programme linking cancer to haemostasis. Nature 434(7031):396-400. DOI: 10.1038/nature03357. PMID: 15772665.

10. Boccaccio C, Ando M, Tamagnone L, Bardelli A, Michieli P, Battistini C, and Comoglio PM. (1998). Induction of epithelial tubules by growth factor HGF depends on the STAT pathway. Nature 391(6664):285-8. DOI: 10.1038/34657. PMID: 9440692.

15 More relevant publications in the last 5 years

1. De Bacco F, Orzan F, Casanova E, Prelli M, and Boccaccio C. (2023). Protocol for in vitro establishment of heterogeneous stem-like cultures derived from whole human glioblastoma tumors. STAR protocols 4(4):102705. DOI: https://doi.org/10.1016/j.xpro.2023.102705. PMID: 37971942.

2. De Bacco F, Orzan F, Crisafulli G, Prelli M, Isella C, Casanova E, Albano R, Reato G, Erriquez J, D'Ambrosio A, Panero M, Dall'Aglio C, Casorzo L, Cominelli M, Pagani F, Melcarne A, Zeppa P, Altieri R, Morra I, Cassoni P, Garbossa D, Cassisa A, Bartolini A, Pellegatta S, Comoglio PM, Finocchiaro G, Poliani PL, and Boccaccio C. (2023). Coexisting cancer stem cells with heterogeneous gene amplifications, transcriptional profiles, and malignancy are isolated from single glioblastomas. Cell Reports 42(8):112816. DOI: 10.1016/j.celrep.2023.112816. PMID: 37505981.

3. Candiello E, Reato G, Verginelli F, Gambardella G, D Ambrosio A, Calandra N, Orzan F, Iuliano A, Albano R, Sassi F, Luraghi P, Comoglio PM, Bertotti A, Trusolino L, and Boccaccio C. (2023). MicroRNA 483-3p overexpression unleashes invasive growth of metastatic colorectal cancer via NDRG1 downregulation and ensuing activation of the ERBB3/AKT axis. Molecular Oncology 17(7):1280-1301. DOI: 10.1002/1878-0261.13408. PMID: 36862005.

4. Brundu S, Napolitano V, Franzolin G, Lo Cascio E, Mastrantonio R, Sardo G, Cascardi E, Verginelli F, Sarnataro S, Gambardella G, Pisacane A, Arcovito A, Boccaccio C, Comoglio PM, Giraudo E, and Tamagnone L. (2023). Mutated axon guidance gene PLXNB2 sustains growth and invasiveness of stem cells isolated from cancers of unknown primary. EMBO Molecular Medicine 15(3): e16104. DOI: 10.15252/emmm.202216104. PMID: 36722641.

5. Orzan F, De Bacco F, Lazzarini E, Crisafulli G, Gasparini A, Dipasquale A, Barault L, Macagno M, Persico P, Pessina F, Bono B, Giordano L, Zeppa P, Melcarne A, Cassoni P, Garbossa D, Santoro A, Comoglio PM, Indraccolo S, Simonelli M, and Boccaccio C. (2023). Liquid Biopsy of Cerebrospinal Fluid Enables Selective Profiling of Glioma Molecular Subtypes at First Clinical Presentation. Clinical Cancer Research 29(7):1252-1266. DOI: 10.1158/1078-0432.CCR-22-2903. PMID: 36648487.

6. Cerqua M, Botti O, Arigoni M, Gioelli N, Serini G, Calogero R, Boccaccio C, Comoglio PM, and Altintas DM. (2022). METΔ14 promotes a ligand-dependent, AKT-driven invasive growth. Life Science Alliance 5(10): e202201409. DOI: 10.26508/lsa.202201409. PMID: 35636967.

7. De Bacco F, Orzan F, Erriquez J, Casanova E, Barault L, Albano R, D'Ambrosio A, Bigatto V, Reato G, Patane M, Pollo B, Kuesters G, Dell'Aglio C, Casorzo L, Pellegatta S, Finocchiaro G, Comoglio PM, and Boccaccio C. (2021). ERBB3 overexpression due to miR-205 inactivation confers sensitivity to FGF, metabolic activation, and liability to ERBB3 targeting in glioblastoma. Cell Reports 36(4):109455. DOI: 10.1016/j.celrep.2021.109455. PMID: 34320350.

8. Verginelli F, Pisacane A, Gambardella G, D'Ambrosio A, Candiello E, Ferrio M, Panero M, Casorzo L, Benvenuti S, Cascardi E, Senetta R, Geuna E, Ballabio A, Montemurro F, Sapino A, Comoglio PM, and Boccaccio C. (2021). Cancer of unknown primary stem-like cells model multi-organ metastasis and unveil liability to MEK inhibition. Nature Communications 12(1):2498. DOI: 10.1038/s41467-021-22643-w. PMID: 33941777

9. Lupo B, Sassi F, Pinnelli M, Galimi F, Zanella ER, Vurchio V, Migliardi G, Gagliardi PA, Puliafito A, Manganaro D, Luraghi P, Kragh M, Pedersen MW, Horak ID, Boccaccio C, Medico E, Primo L, Nichol D, Spiteri I, Heide T, Vatsiou A, Graham TA, Elez E, Argiles G, Nuciforo P, Sottoriva A, Dienstmann R, Pasini D, Grassi E, Isella C, Bertotti A, and Trusolino L. (2020). Colorectal cancer

residual disease at maximal response to EGFR blockade displays a druggable Paneth cell-like phenotype. Science Translational Medicine 12(555):eaax8313. DOI: 10.1126/scitranslmed.aax8313. PMID: 32759276.

10. Benvenuti S, Milan M, Geuna E, Pisacane A, Senetta R, Gambardella G, Stella GM, Montemurro F, Sapino A, Boccaccio C, and Comoglio PM. (2020). Cancer of Unknown Primary (CUP): genetic evidence for a novel nosological entity? A case report. EMBO molecular medicine 12(7):e11756. DOI: 10.15252/emmm.201911756. PMID: 32511869.

11. Orzan F, Pagani F, Cominelli M, Triggiani L, Calza S, De Bacco F, Medicina D, Balzarini P, Panciani PP, Liserre R, Buglione M, Fontanella MM, Medico E, Galli R, Isella C, Boccaccio C, and Poliani PL. (2020). A simplified integrated molecular and immunohistochemistry-based algorithm allows high accuracy prediction of glioblastoma transcriptional subtypes. Laboratory investigation 100(10):1330-1344. DOI: 10.1038/s41374-020-0437-0. PMID: 32404931.

12. Simonelli M, Dipasquale A, Orzan F, Lorenzi E, Persico P, Navarria P, Pessina F, Nibali MC, Bello L, Santoro A, and Boccaccio C. (2020). Cerebrospinal fluid tumor DNA for liquid biopsy in glioma patients' management: Close to the clinic? Critical reviews in oncology/hematology 146:102879. DOI: 10.1016/j.critrevonc.2020.102879. DOI: 10.1016/j.critrevonc.2020.102879.

13. Gallo S, Spilinga M, Albano R, Ferrauto G, Di Gregorio E, Casanova E, Balmativola D, Bonzano A, Boccaccio C, Sapino A, Comoglio PM, and Crepaldi T. (2020). Activation of the MET receptor attenuates doxorubicin-induced cardiotoxicity in vivo and in vitro. British journal of pharmacology 177(13):3107-3122.

14. Comoglio PM, Trusolino L, and Boccaccio C. (2018). Known and novel roles of the MET oncogene in cancer: a coherent approach to targeted therapy. Nature Reviews Cancer 18(6):341-358. DOI: 10.1038/s41568-018-0002-y. PMID: 29674709.

15. Luraghi P, Bigatto V, Cipriano E, Reato G, Orzan F, Sassi F, De Bacco F, Isella C, Bellomo SE, Medico E, Comoglio PM, Bertotti A, Trusolino L, and Boccaccio C. (2018). A Molecularly Annotated Model of Patient-Derived Colon Cancer Stem-Like Cells to Assess Genetic and Nongenetic Mechanisms of Resistance to Anti-EGFR Therapy. Clinical cancer research 24(4):807-820. DOI: 10.1158/1078-0432.CCR-17-2151. PMID: 28974546.

Autorizzo il trattamento dei miei dati personali presenti nel CV ai sensi dell'art. 13 d. lgs. 30 giugno 2003 n. 196 - "Codice in materia di protezione dei dati personali" e dell'art. 13 GDPR 679/16 - "Regolamento europeo sulla protezione dei dati personali".

Candiolo, 21/11/2023

Carla Boccaccio