Andrea Bertotti

CURRICULUM VITAE

Personal information

Researcher unique identifier: Author ID: 6603084027 (Scopus); 0000-0001-8196-7608 (ORCID)
Date of birth: January 20th, 1977
Nationality: Italian

Education and training

1995 – 2001: University of Torino School of Medicine, Torino, Italy. Full honours and special award.
2001 – 2006: Ph.D. in Cellular Biology, University of Torino, Torino, Italy.
2006 – 2010: Post-doctoral training, Candiolo Cancer Institute, Candiolo, Torino, Italy.

Positions and employment:

2017: Associate Professor, University of Torino School of Medicine, Torino, Italy.
2010: Assistant Professor, University of Torino School of Medicine, Torino, Italy.
2008: Co-head, Laboratory of Translational Cancer Medicine, Candiolo Cancer Institute, Candiolo, Torino, Italy.

RESEARCH INTERESTS

Almost two decades ago, the human genome project was completed. Concomitantly, the first striking evidence of efficacy for targeted therapies was provided by treatment of Philadelphia chromosome-positive chronic myelogenous leukaemia with imatinib. Since then, a plethora of candidate targets have been discovered, and drugs proposed to treat solid and liquid neoplasms. However, almost 20 years after the initial premises, how and why a tumour will initially respond to therapy and, even more important, when and by which means it will eventually relapse remains largely unknown.

I have been always profoundly convinced that the relative unsuccess of targeted therapies can be, at least partially, ascribed to the lack of quantitative and objective experimental approaches amenable to tackle the issue. Therefore, my research for the last 10 years has been focused on the development of new approaches and methods to incorporate quantitative and statistically robust methods into preclinical research pipelines oriented at understanding the molecular principles of response and resistance to targeted therapies.

To this aim, I set up an experimental platform for high-fidelity anticipation of clinical responses at the population level through the extensive use of patient-derived xenografts (PDXs). We have used colorectal cancer as a model system to demonstrate that, when combining stringent analytical conditions and large-scale experiments, PDXs can very effectively recapitulate the behaviour of real patients. To achieve this, I coordinated the deployment of a unique informatics platform for the integrated management of multidimensional data from patients, xenografts and cell lines. My next goal is to leverage the informative potential of this platform to gather new insights into the evolutionary dynamics of metastatic disease.

Current research topics include:

- The mechanistic bases of synergism in drug combinations.
- The identification of cancer vulnerabilities emerging as a consequence of adaptation to primary therapies.
- Tumour genetic evolution and involution during response to targeted therapies.
- Drug tolerance and phenotypic adaptation in residual disease.
- The relationship between cytostasis and apopotosis in response to targeted drugs.

MAJOR ACHIEVEMENTS

During the past 15 years I have focused my research on dissecting and targeting tyrosine-kinase dependent signals in cancer.

As a Ph.D. student, I contributed to extending the classical approaches of molecular oncology to the field of cell-matrix interactions. This resulted in the publication of several papers reporting the functional contribution of integrins to tyrosine kinase-regulated biological activities in cancer (Trusolino*, Bertotti* and Comoglio, *Cell* 2001 [*equal contributors]; Bertotti and Comoglio, *Trends Biochem. Sci.* 2003; Bertotti et al., *Cancer Res.* 2005; Bertotti et al., *J. Cell Biol*. 2006).

In the post-doctoral period, I broadened my research interests to systems biology approaches, which I exploited to illustrate the global consequences of receptor tyrosine kinase inhibition in oncogene-addicted cells (Bertotti et al., *Sci. Signal.* 2009). Those studies were fundamental to fully realise the potential inherent to multi-dimensional molecular profiling of cancer and motivated my interest in finding original ways to overcome the limitations of cell line-based approaches for understanding cancer at the systems level.

Prompted by this interest, as a post-doctoral fellow I set up a platform of PDXs – currently the largest PDX resource available in an academic environment – as tools for performing genotype/response correlations and discovering novel therapeutic targets, with an emphasis on colorectal cancer. Such initiative paved the way for new approaches to translational research, allowing for unprecedented preclinical analyses of response determinants on a population scale.

Starting 2011, I launched – and I am still coordinating – a team of software engineers for the development of the Laboratory Assistant Suite (LAS), a web-based application that assists biomedical researchers in multiple activities, which range from tracking data generation and SOPs execution to the management of multidimensional molecular profiles (Baralis et al., *J. Med. Syst.* 2011). A testimony to my inclination for multi-disciplinary research, this asset confers high added value to our experimental approach and has supported successful execution of extensive in vivo studies, which have become leading references in the field (see for example Gao et al., *Nat. Med.* 2015).

By exploiting the collection of PDXs set up in my laboratory, my group was able to discover and functionally validate a number of biomarkers predicting response or resistance to EGFR blockade. This led to 8 publications in high-profile journals in which my primary contribution was acknowledged by first, last and/or corresponding authorships (Bertotti et al., Cancer Discov. 2011; Galimi et al., Clin. Cancer Res. 2011; Migliardi et al., Clin. Cancer Res. 2012; Bardelli et al., Cancer Discov. 2013; Kavuri et al., Cancer Discov. 2015; Leto et al., Clin. Cancer Res. 2015; Zanella et al., Sci. Transl. Med. 2015; Bertotti et al., Nature 2015). As an attestation to these efforts, our discovery that HER2 amplification predicts resistance to anti-EGFR antibodies and sensitivity to anti EGFR/HER2 treatment in colorectal cancer (Bertotti et al., Cancer Discov. 2011) was translated into HERACLES, a successful phase II clinical trial (Sartore-Bianchi et al., Lancet Oncology. 2016). This study has provided the best proof-of-concept supporting the feasibility and efficacy of my approach, with more than 30% objective response rate in heavily pre-treated patients.

AWARDS

2017: ERC Consolidator Grant – ERC.
2015: Andrea e Libi Lorini award, early careers in oncology – Fondazione Lorini.
2014: NextGenStar award – AACR.
2012: Fight Colorectal Cancer award in memory of Lisa Dubow, Career development award – AACR.
2007: Lucatello e Mazzega award – AIRC (Associazione Italiana per la Ricerca sul Cancro).
2001: Best MD thesis – University of Torino School of Medicine.

PEER-REVIEWING ACTIVITY

Grant reviewer for the Swiss National Science Foundation.

Ad-hoc peer-reviewer for Nature Pathway Interaction Database, Journal of Cell Biology, Cancer Research, Clinical Cancer Research, Oncogene, Journal of Cell Science, BMC Cancer, Journal of Biological Chemistry, Cancer Prevention Research, Breast Cancer Research, Molecular Cancer, Molecular Oncology, PLoS One, Cancer Letters, Journal of Clinical Pathology, Faseb Journal, Carcinogenesis.

PUBLICATION METRICS

I have published 48 papers in peer-reviewed international journals, including 41 original research papers (18 as first/last/corresponding author), 4 invited reviews (2 as first/last/corresponding author), and 3 invited editorials/commentaries (all as first/last/corresponding author).

Total Impact Factor (IF, Thomson Reuters 2017 release): 649. Average IF: 13.5. Total IF first/last/corresponding author: 345 (53%). Average IF first/last/corresponding author: 15.0.

Total citations in Scopus (June 2017): 2636. Total citations first/last/corresponding author: 1413 (53%).

H-index (Scopus, January 2018): 26.

INVITED PRESENTATIONS (selected, 2012 – 2017)

2017: EACR-AACR-SIC. June 24-27, Florence, Italy.
2017: Charles River's 8th European Short Course. March 22-24, Berlin, Germany.
2016: EurOPDX meeting 2016. October 3-5, Weggis, Switzerland.
2016: AACR Special Conference on Patient Derived Cancer Models: Present and Future Applications from Basic Science to the Clinic. February 11-14, New Orleans, LA.
2014: AACR Annual meeting 2014a. April 5-9, San Diego, CA.
2014: AACR Annual meeting 2014b. April 5-9, San Diego, CA.
2014: Charles River's 7th European Short Course. February 12-14, Strasbourg, France.
2012: NSABP Annual Division of Industry Trials Fall Investigator Meeting. October 18-19,Chicago, IL.