

BIOGRAPHICAL SKETCH

NAME: **Prof Filippo Acconcia**

eRA COMMONS USER NAME (credential, e.g., agency login): **not available**

POSITION TITLE: **Associate Professor of Physiology**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University Roma TRE, Rome Italy	Ph. D	01/2002-12/2004	Estrogen-dependent Regulation of Cell Proliferation in Cancer Cells
<i>Institut Jules Bordet, Universite Libre de Bruxelles, Bruxelles Belgium</i>	<i>Visiting Scientist</i>	<i>10/2004</i>	<i>Proteasome-mediated Degradation of the Estrogen Receptor alpha in Breast Cancer Cells</i>
MD Anderson Cancer Center, Houston, Texas, USA	Postdoctoral	01/2005-10/2006	Estrogen Receptor alpha Signalling in Breast Cancer Cell Proliferation and Migration
<i>IFOM - Istituto Fondazione di Oncologia Molecolare, Milan, Italy</i>	<i>Postdoctoral</i>	<i>10/2006-10/2008</i>	<i>Ubiquitin Signalling in EGFR Endocytosis and in Breast Cancer Cell Migration</i>

A. Personal Statement

My primary research interest is understanding how cells sense environmental challenges and decode the information in the stimulus' strength, converting it into an intracellular cascade of molecular events that ultimately regulate several physiological processes (e.g., cell proliferation and migration). My research focuses on analyzing the molecular mechanisms induced by 17 β -estradiol (E2) through its binding to estrogen receptor alpha (ER α) and estrogen receptor beta (ER β). A detailed evaluation of the molecular mechanisms underlying the physiological actions of E2 is critical for identifying new targets for the treatment of endocrine-related pathologies, including cancer. In recent years, my interest has shifted towards breast cancer (BC) expressing ER α , with a particular focus on metastatic BC, which expresses specific ER α point mutations that confer resistance to classic endocrine therapy drugs. Recently, we have discovered drugs that specifically act on different types of BC and are actively searching for compounds that could be selectively used based on the specific ER α variant expressed in MBC.

B. Positions, Scientific Appointments, Honors, and Funding ID

Positions and Scientific Appointments

2015–Present: Associate Professor, Department of Science Section Biomedical Science and Technology, University Roma TRE, Rome, Italy.

2008–2015: Assistant Professor, Department of Science Section Biomedical Science and Technology, University Roma TRE, Rome, Italy.

2006 – 2009: Three-year fellowship from AIRC (Associazione Italiana Ricerca sul Cancro).
2004-Present: Member of the Italian Society of Physiology (SIF).
2019-Present: Member of the Associazione per la Biologia Cellulare e del Differenziamento (ABCD).
2019-Present: Member of the Italian Society for Cancerology.
2009-Present: Participation in the Doctoral College of Biology Applied to Human Health and Biomedical Sciences and Technologies at Roma TRE University. Recently, I also assumed the position of deputy director.

Honors

2023: Habilitation Degree to Full Professor of Applied Biology (validity:2023-2034);
2023: Habilitation Degree to Full Professor of Physiology (validity:2023-2034)
2019-2022: GEV Member of the Scientific Area 05/D1 SSD BIO/09 for the evaluation activities within the VQR 2015-2019 exercise concerning the scientific products or third mission case studies submitted by the evaluated institutions.
2018: Invitation to be a Member of the Evaluation Committee in the final examination for Mr Ali CHOUCAIR' s Ph D Thesis at the Université Claude Bernard Lyon 1, France in the Laboratory of Prof Muriel LeRomancer.
2017: Habilitation Degree to Full Professor of Physiology (validity:2017-2028)
2016: Invitation to be a Member of the Evaluation Committee in the final examination for Mr Soleilmane OMARJEE' s Ph D Thesis at the Université Claude Bernard Lyon 1, France in the Laboratory of Prof Muriel LeRomancer.
2015: Prize from the Italian Physiological Society. Best Young Researcher 2015.
2015: Associate Editor for Frontiers in Physiology – Membrane Physiology and Membrane Biophysics.
2013: Ambassador for the European Association for Cancer Research.
2006: Amgen Poster Award MD Anderson Cancer Center Houston Texas, USA. Best Poster in basic science in cancer research.

Funding ID

2022: Operative Unit of the funded project 'ENDORSEMENT OF MKK3 AS NOVEL PROGNOSTIC BIOMARKER AND THERAPEUTIC TARGET IN ADVANCED COLORECTAL CANCER' RF-2021-12372851
2019-2023: Recipient of the AIRC IG21325 - 5 years entitled 'New Drugs for ER α Primary and Metastatic Breast Cancer'
2015-2018: Recipient of the AIRC MFAG12765 2012 - 3 years entitled 'Investigating breast cancer: the role of estrogen receptor alpha (ER α) intracellular trafficking'.

Activity as Invited Reviewer for International Scientific Journal

Prof Filippo Acconcia works as Invited referee for different peer reviewer's journals including SCIENTIFIC REPORTS, GENE AND NUTRITION, JOURNAL OF ENDOCRINOLOGY, BMC CANCER, JOURNAL OF NUTRITION, JOURNAL OF MOLECULAR ENDOCRINOLOGY, MOLECULAR AND CELLULAR ENDOCRINOLOGY, TREND IN ENDOCRINOLOGY AND METABOLISM.

C. Contributions to Science

The following is a list of Professor Filippo Acconcia's (FA) major scientific accomplishments:

1-Definition of the molecular bases for ER α plasma membrane association and signaling. FA discovered that ER α is lipid-modified with palmitic acid at cysteine residue 447. Moreover, FA demonstrated that ER α palmitoylation is necessary for receptor plasma membrane localization and the activation of rapid E2-induced signaling and downstream cellular processes (e.g., cell proliferation and cell migration). FA's work defined a novel circuitry by which ER α palmitoylation links E2-dependent ER α degradation, ER α phosphorylation, and transcriptional activity in a unique molecular mechanism in BC cells. Such advances in the basic knowledge of E2 signaling have provided new druggable targets for the treatment of BC (1-6).

Prof Filippo Acconcia

2-Determination that proteolytic and non-proteolytic ER α ubiquitination is critical for E2:ER α signaling-induced cell proliferation. FA discovered that E2-induced cell proliferation requires ER α mono-ubiquitination, which negatively regulates ER α activity. In addition, FA determined that E2 negatively modulates ER α mono-ubiquitination and that this posttranslational modification does not occur on ER β . FA also discovered two ubiquitin (Ub) binding surfaces (UBS) within ER α that trigger a non-covalent Ub:ER α association. FA demonstrated that the ER α UBS located within the receptor ligand binding domain is required for ER α signaling-regulated cell proliferation through activation of the PI3K/AKT/CREB1 axis and that the non-covalent Ub-binding of ER α controls E2 signaling. FA's discoveries indicate that interfering with the ER α UBS:Ub interaction through small molecules or peptides could represent a novel druggable target for BC treatment (7-14).

3-Discovery that endocytic proteins are critical for E2:ER α signaling-induced cell proliferation. FA discovered a novel way by which BC cells control ER α degradation. FA determined that E2 triggers ER α localization to lysosomes and degradation through complex ER α intracellular trafficking that involves association with clathrin heavy chain (CHC). E2 rapidly induces the ER α :CHC interaction, which occurs in the cytoplasm of BC cells. This interaction is required for E2:ER α signaling-induced cell proliferation. In addition, FA discovered that diverse endocytic proteins (e.g., caveolin-1, caveolin-2, AP2, and dynamin II) play critical roles in regulating E2 signaling in BC cells. Consequently, FA's work has provided a previously unrecognized molecular mechanism by which E2 controls BC cell proliferation and BC progression (15-19).

4-Discovery of novel anti-ER α BC drugs through the selective modulation of ER α levels and degradation. FA identified a new pharmacological target in BC cells: the modulation of intracellular ER α levels. Indeed, FA unveiled that whatever causes an imbalance in ER α levels (e.g., ligands/molecules or pathways) has the potential to inhibit the E2-dependent proliferation of BC cells. Thus, FA exploited this point of weakness for therapeutic purposes to identify compounds whose administration block ER α -positive BC progression. Based on these notions, FA applied different libraries of compounds in a new antiestrogen discovery platform (AWARD) to ER α expressing cells modeling primary and MBC. Through this approach, FA fished out several drugs and kinase inhibitors with an apparent activity superimposable/superior to that of fulvestrant (Ful). Therefore, FA's recent discoveries provide new hopes for patients with BC by suggesting a re-purposing use of those compounds for alternative treatment of primary and MBC (20-36).

Complete List of Published Work in PubMed.

Prof Filippo Acconcia is Author of 77 scientific publications (<https://pubmed.ncbi.nlm.nih.gov/?term=Acconcia+F>), all published in International Peer-Reviewer's Journals. Prof Filippo Acconcia (Orcid: 0000-0002-4651-2509) has 37 as h-index and a total number of citations > of 4,400 (Scopus ID: 6505820454).

Citations

- 1.La Rosa P, et al.: *Mol Endocrinol* 2012;26:762. DOI: [10.1210/me.2011-1208](https://doi.org/10.1210/me.2011-1208).
- 2.Acconcia F, et al.: *J Cell Physiol* 2005;203:193. DOI: [10.1002/jcp.20219](https://doi.org/10.1002/jcp.20219).
- 3.Acconcia F, et al.: *Molecular Biology of the Cell* 2005;16:231. DOI: [10.1091/mbc.E04-07-0547](https://doi.org/10.1091/mbc.E04-07-0547).
- 4.Acconcia F, et al.: *Biochem Biophys Res Commun* 2004;316:878. DOI: [10.1016/j.bbrc.2004.02.129](https://doi.org/10.1016/j.bbrc.2004.02.129).
- 5.Acconcia F, et al.: *Iubmb Life* 2003;55:33. DOI: [10.1080/1521654031000081256](https://doi.org/10.1080/1521654031000081256).
- 6.Acconcia F, et al.: *Mol Cell Endocrinol* 2021;538:111452. DOI: [10.1016/j.mce.2021.111452](https://doi.org/10.1016/j.mce.2021.111452).
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- 8.La Rosa P, et al.: *Cellular Signalling* 2011;23:1128. DOI: [10.1016/j.cellsig.2011.02.006](https://doi.org/10.1016/j.cellsig.2011.02.006).
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- 12.Pesiri V, et al.: *IUBMB Life* 2014;66:578. DOI: [10.1002/iub.1296](https://doi.org/10.1002/iub.1296).
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- 14.Pesiri V, et al.: *IUBMB Life* 2016;68:569. DOI: [10.1002/iub.1514](https://doi.org/10.1002/iub.1514).
- 15.Pesiri V, et al.: *Immunology, Endocrine and Metabolic Agents in Medicinal Chemistry* 2014;14:75.

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19. Totta P, et al.: *PLoS One* 2014;9:e94880. DOI: [10.1371/journal.pone.0094880](https://doi.org/10.1371/journal.pone.0094880).
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