



ELENA SACCO, PhD

Department of Biotechnology and Biosciences (BtBs), University of Milano-Bicocca (UNIMIB).
Piazza della Scienza, 2, 20126 Milano, Italy. Phone: +39.02.64483379, E-mail: elena.sacco@unimib.it

Present positions

- Assistant Professor in 05/E1 (Biochemistry) at BtBs, University of Milano-Bicocca
- Member of SIB (Società Italiana di Biochimica e Biologia Molecolare)
- Member of ISBE (Infrastructure for Systems Biology Europe)
- Member of Best4Food (Bicocca cEnter of Science and Technology for FOOD)
- Member of 3R Center (Center for Replacement, Reduction and Refinement in animal research),
- Member of Center for neuroscience: NeuroMI, University of Milano-Bicocca
- Member of PhD Course in Converging Technologies for Biomolecular Systems (TeCSBi), University of Milano-Bicocca.
- Member of commission of CHRONOS LID of Multicellular Advanced models at BtBs, University of Milano-Bicocca.
- Coordinator of “Progetto Piano Lauree Scientifiche di Biologia e Biotecnologie”, University of Milano-Bicocca, Milano, Italy. Third mission.

Research fields

- Characterization and targeting of metabolism, redox homeostasis and Ras signaling in 2D and 3D preclinical cellular models of cancer in the perspective of precision medicine.
- Multiscale analysis from structure to intracellular regulatory network of biological systems under physiopathological- or environmental perturbation conditions (topics: Ras-transformation, cancer metabolism, neurofibromatosis, chemoresistance).
- Analysis of potency, selectivity and mechanism of action of small molecules, on purified proteins, cell lysates and 2D and 3D cellular models (synthetic Ras inhibitors and Natural Products including Green coffee, Cacao, Vigna Unguiculata and *Cannabis sativa* derivatives).

Main research projects ongoing

- Research & Development of Ras inhibitors as anticancer agents (funded by Italian Ministry of University and Research (MIUR) through grants “Research facilitation fund (Fondo per le Agevolazioni alla Ricerca-FAR, Project AIMS™ AWARDS)
- Profiling and targeting of energy and redox metabolism in bladder cancer (funded in the context of AMPLITUDE grant, PI-Prof. Vanoni and by Dott. Vago IRCCS San Raffaele Scientific Institute)
- Establishment and characterization of Breast Cancer Patient-specific cellular, animal and computational models for developing personalised drug treatment targeting metabolism. (funded in the context of IT:FOC-Information Technology: The future of cancer treatment - FLAG-ERA (PI-Prof. Alberghina, Prof. Vanoni)
- Multilevel computational approach for the identification of the functional network of neurofibromin type 1 in nervous system.

Education

- Dec 2002:** PhD in Industrial Biotechnology, University of Milano-Bicocca, Italy.
- May 1997:** Master Degree in Biological Sciences (110/110 cum laude), University of Milano, Italy.

Previous appointments, awards and research positions

- 2010–present:** permanent position as Assistant Professor at BtBs UNIMIB (Biochemistry);
Multiscale approach for the identification of regulatory biological circuits

- 2008-2010:** winner of a government post-doc fellowship at BtBs UNIMIB; *Ras signaling: clinical target in proliferative disorders*
- 2007:** Winner of a public contest for 1-year post-doc fellowship as PI in 'Iniziativa Ingenio', FinLombarda Spa, Regione Lombardia, in 2007; *Development of Ras inhibitors*
- 2006:** post-doc fellow of Associazione Levi-Montalcini at BtBs UNIMIB; *Drug design*
- 2002-2005:** Winner of public contest for a 3-years post-doctoral fellowship from FIRC Unicredito Italiano 2003-2005 on cancer research at BtBs UNIMIB; *Ras-dependent carbon metabolism and transformation in mouse fibroblasts*
- 1999-2002:** 3-years PhD Italian government fellowship at BtBs UNIMIB; *Structure/function relationships of Ras-specific GEFs*
- 1997-1999:** fellow of Norpharma Spa/Biopolo at the Dept. of Physiology and Biochemistry, University of Milano; *Protein engineering*

Research activities, competences and technical skills

For years, ES has been involved in research activities in collaboration with Prof. Marco Vanoni and Prof. Lilia Alberghina, driving force for the development of Systems Biology in Italy and Europe. ES performed: structure/function studies of Ras-specific mammalian GEFs (Greco et al., 2005; Sacco et al., 2006; Sacco et al., 2010; Sacco et al., 2012a); analysis of molecular bases of Ras-transformation and metabolic rewiring (Chiaradonna et al., 2005; Chiaradonna et al., 2006; Vanoni et al., 1999; De Sanctis et al., 2016); rational design, development and characterization of Ras inhibitors with anticancer properties (Sacco et al., 2005; Palmioli et al., 2009; Sacco et al., 2011; Sacco et al., 2012b; Palmioli et al., 2017; Tisi et al., 2021), even derived from complex sources as plant extracts; analysis of the RAS/PKA pathway (Magherini et al., 2006) and reconstruction of the EGF-R signaling pathway in yeast *S. cerevisiae* (Busti et al., 2008). ES engineered proteases from yeast and archaeobacteria for industrial applications of targeted proteolysis. ES has studied the complex network regulating DNA replication initiation in yeast and mammals (Sacco et al., 2012c) and she has performed a multiscale analysis from structure to intracellular regulatory and functional network of Whi5 and Rb proteins (Hasan et al., 2014). ES has expertise in studying complex intramolecular interactions-based regulatory networks, and she has considerable knowledge of Ras signaling and human disorders associated with its deregulation (Sacco et al., 2012d, Tisi et al., 2020), and System Biology integrative multi-omics approach for clinical application (De Sanctis et al., 2018, Damiani et al., 2020). ES has also expertise in designing and applying multi-level approaches for the identification of regulatory networks of complex biological systems, from molecular and biochemical analysis to concept map construction, towards mathematical modeling and simulation (manuscript in preparation). ES has explored the molecular basis of tunneling nanotubes in bladder cancer (D'Aloia et al., 2021) and the effect of cannabidiol in triple negative breast cancer cells (D'Aloia et al., 2022). ES has recently focused its research on cancer metabolism profiling and targeting, applying different methodological approaches including Seahorse and high-content confocal analysis to 2D and 3D cellular models of solid tumors (Denise et al., 2015; Pasquale et al., 2020, Raggi et al., 2021; Sforza et al. 2022; Campioni et al. 2022).

Human and technical skills

During her career ES has supervised several undergraduate, graduate and PhD students, gaining experience in human resources management. She has technical skills in DNA recombinant and molecular biology methods, mammalian cell cultures, protein/protein interaction (Biacore technology) and enzyme assays, FACS analysis; Fluorescence and Confocal Microscopy; Seahorse technology; Use of bioinformatic tools for 3D structure, biosequence, protein-protein interaction analysis, modeling and simulation of complex biological systems.

Grants

- Grant EU 7FP UNICELLSYS Eukaryotic unicellular organism biology: system biology of the control of cell growth and proliferation (2008-2013). Partner 10 UNIMIB-Subunit 2 (PI: Marco Vanoni) Role: participant.
- Grant RBPR05ZK2Z of the Italian Government (FIRB) Italbionet -Italian Bioinformatic Network (2007-2013). (Coordinator: Prof. A. Albertini). Subunit UNIMIB (PI: Prof. L. Alberghina). Role: participant.
- Grant from Creabilis Therapeutics Spa (2007-2008): *Development of RasGRF derivatives as anticancer agents* (PI: Prof M. Vanoni) Role: participant.
- AIMS AWARD: Identification of inhibitors of that selectively target Oncogenic mutant RasG13D (2019) Role: PI.
- Grant EU FLAG-ERA Information Technology: Future of Cancer Treatment ITFoC, Topic: Digital Medicine for Cancer (PI: Prof Alberghina) Role: participant
- Grant Horizon 2020 Amplitude n. 871277 grant. (PI: Marci Vanoni) Role: participant

Publications

29 papers on peer-reviewed international journals; 4 scientific book chapters, and several participations in national and international congresses.

Total publications: 32 Total citations: 477; H index =12; (Scopus, June 2022).

Corresponding authors

- P1. M. Vanoni, R. Bertini, **E. Sacco**, L. Fontanella, M. Rieppi, S. Colombo, E. Martegani, V. Carrera, A. Moroni, C. Bizzarri, V. Sabbatini, M. Cattozzo, A. Colagrande, and L. Alberghina (1999) Characterization and properties of dominant negative mutants of the ras-specific guanine nucleotide exchange factor CDC25Mm. *Journal of Biological Chemistry* 274(51): 36656-662
- P2. **E. Sacco**, P. Tortora and M. Vanoni (2004) Archaeal serine proteases. *Handbook of proteolytic enzymes* 2nd Edn 562. 1819-1823
- P3. F. Chiaradonna, C. Magnani, **E. Sacco**, R. Manzoni, L. Alberghina and M. Vanoni (2005) Acquired glucose sensitivity of k-ras transformed fibroblasts. *Biochemical Society Transactions* 33: 297-299
- P4. C. Greco, **E. Sacco**, M. Vanoni and L. De Gioia (2005) Identification and in silico analysis of a new group of double histone fold containing proteins. *Journal of molecular modeling* (Online) 1-9
- P5. F. Magherini, S. Busti, T. Gamberi, **E. Sacco**, G. Raugei, G. Manao, A. Modesti, G. Ramponi, M. Vanoni (2005) In *Saccharomyces cerevisiae* an unbalanced level of tyrosine phosphorylation down-regulates the Ras/PKA pathway. *The International Journal of Biochemistry and Cell Biology* 38 (3): 444-460
- P6. **E. Sacco**, S. Fantinato, R. Manzoni, D. Metalli, L. De Gioia, P. Fantucci, L. Alberghina and M. Vanoni (2005) The isolated catalytic hairpin of the Ras-specific Guanine nucleotide Exchange Factor Cdc25Mm retains nucleotide dissociation activity but has impaired nucleotide exchange activity. *FEBS Letters* 579: 6851-6858
- P7. F. Chiaradonna, **E. Sacco**, R. Manzoni, M. Giorgio, M. Vanoni and L. Alberghina (2006) Ras dependent carbon metabolism and transformation in murine fibroblast. *Oncogene* 25 (39): 5391-5404
- P8. **E. Sacco**, D. Metalli, S. Busti, S. Fantinato, A. D'Urzo, V. Mapelli, L. Alberghina and M. Vanoni (2006) Catalytic competence of the Ras-GEF domain of hSos1 requires intra-REM domain interactions mediated by Phenylalanine 577 *FEBS Letters* 580 (27): 6322-6328
- P9. S. Busti, E. Sacco, E. Martegani and M. Vanoni (2008) Functional coupling of the mammalian EGF receptor to the Ras/cAMP pathway in the yeast *Saccharomyces cerevisiae* *Curr Genet* 53 (3): 153-162.
- P10. A. Palmioli, **E. Sacco**, S. Abraham, C.J. Thomas, A. Di Domizio, L. De Gioia, V. Gaponenko, M. Vanoni, and F. Peri (2009). First experimental identification of Ras-inhibitor binding interface using a water-soluble Ras ligand. *Bioorg Med Chem Lett* 19: 4217-4222. <http://www.sciencedirect.com/science/article/pii/S0960894X09008002>
- P11. A. Palmioli¹, **E. Sacco**¹, C. Airolidi, F. Di Nicolantonio, A. D'Urzo, S. Shirasawa, T. Sasazuki, A. Di Domizio, L. De Gioia, E. Martegani, F. Peri and M. Vanoni (2009). Selective cytotoxicity of a bicyclic Ras inhibitor in cancer cells expressing K-Ras(G13D). *Biochemical and biophysical research communications* 386: 593-597. ¹first authors <http://www.sciencedirect.com/science/article/pii/S0006291X09012133>
- P12. **E. Sacco**¹, M. Farina¹, C. Greco, S. Busti, D. Spiliotopoulos, L. DeGioia, D. Liberati, L. Alberghina, M. Vanoni (2010). The regulation of hSos1 as an emergent property of its multi-domain structure: molecular and computational analysis. *Biomedical Signal-Image Processing and Modelling* 09_1 ¹first authors. Not peer reviewed journal.
- P13. **E. Sacco**, S.J. Abraham, A. Palmioli, G. Damore, A. Bargna, E. Mazzoleni, V. Gaponenko, M. Vanoni, F. Peri (2011). Binding properties and biological characterization of new sugar-derived Ras ligands. *Med. Chem. Commun.* 2: 396-401. <http://pubs.rsc.org/en/content/articlelanding/2011/MD/c0md00264j>
- P14. **E. Sacco**, M.E Regonesi, M. Vanoni. (2011) Archaeal serine proteases. *Handbook of proteolytic enzymes* 3rdEdn Chapter 711. pag 3224 Edited by N.D. Rawlings and G.S. Salvesen
- P15. M.E. Regonesi, **E. Sacco**, P. Tortora. (2011) Carboxypeptidase Ss1. *Handbook of proteolytic enzymes* 3rdEdn Chapter 363. pag 1608 Edited by N.D. Rawlings and G.S. Salvesen
- P16. **E. Sacco**¹, M. Farina¹, C. Greco, S. Lamperti, S. Busti, L. DeGioia, L. Alberghina, D. Liberati, M. Vanoni (2012). Regulation of hSos1 activity is a system-level property generated by its multi-domain structure. *Biotechnology advances* 30(1):154-68. ¹first authors <http://www.sciencedirect.com/science/article/pii/S0734975011001273>
- P17. **E. Sacco**, M.M. Hasan, L. Alberghina, M. Vanoni (2012). Comparative analysis of the molecular mechanisms controlling the initiation of chromosomal DNA replication in yeast and in mammalian cells. *Biotechnology advances* 30(1):73-98. <http://www.sciencedirect.com/science/article/pii/S0734975011001625>
- P18. **E. Sacco**, D. Metalli, M. Spinelli, R. Manzoni, M. Samalikova, R. Grandori, A. Morrione, S. Traversa, L. Alberghina, M. Vanoni (2012). Novel RasGRF1-derived Tat-fused peptides inhibiting Ras-dependent proliferation and migration in mouse and human cancer cells. *Biotechnology advances*. 30(1):233-43. <http://www.sciencedirect.com/science/article/pii/S0734975011000668>

- P19. **E. Sacco**, M. Spinelli, **M. Vanoni** (2012) Approaches to Ras signaling modulation and treatment of Ras-dependent disorders: a patent review (2007--present). *Expert Opin Ther Pat.* 22(11):1263-87 <http://www.ncbi.nlm.nih.gov/pubmed/23009088>
- P20. M.M. Hasan, S. Brocca, **E. Sacco**, M. Spinelli, E. Papaleo, M. Lambrughi, L. Alberghina, M. Vanoni (2014). A comparative study of Whi5 and retinoblastoma proteins: from sequence and structure analysis to intracellular networks. *Front Physiol.* 2014, 4:315. doi: 10.3389/fphys.2013.00315. eCollection 2013. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3897220/>
- P21. C. Denise, P. Paoli, M. Calvani, M.L. Taddei, E. Giannoni, S. Kopetz, S.M. Kazmi, M.M. Pia, P. Pettazzoni, **E. Sacco**, A. Caselli, M. Vanoni, M. Landriscina, P. Cirri, P. Chiarugi (2015) 5-Fluorouracil resistant colon cancer cells are addicted to OXPHOS to survive and enhance stem-like traits. *Oncotarget.* 2015 Dec 8;6(39):41706-21. doi: 10.18632/oncotarget.5991.PMID:26527315
- P22. G. De Sanctis, M. Spinelli, M. Vanoni, **E. Sacco** (2016) K-Ras Activation Induces Differential Sensitivity to Sulfur Amino Acid Limitation and Deprivation and to Oxidative and Anti-Oxidative Stress in Mouse Fibroblasts. *PLoS One.* 2016 Sep 29;11(9):e0163790. doi: 10.1371/journal.pone.0163790. eCollection 2016. PMID:27685888
- P23. A. Palmioli, C. Ciaramelli, R.A. Tisi; M. Spinelli, G. De Sanctis, **E. Sacco**, C. Airoidi (2017) Natural compounds in cancer prevention: effects of coffee extracts and their main polyphenolic component 5-CQA on oncogenic Ras proteins. *Chemistry - An Asian Journal*, 12(18), 2457-2466. PMID: 28719146 DOI: 10.1002/asia.201700844
- P24. G. De Sanctis, C. Damiani, **E. Sacco**, M. Vanoni (2018). *Omics and Clinical Data Integration*. DOI:10.1002/9781119183952.ch15. pp.248-273. In *Integration of Omics Approaches and Systems Biology for Clinical Applications* - ISBN:9781119181149 Ed. Wiley
- P25. C. Damiani, D. Gaglio, **E. Sacco**, L. Alberghina, **M. Vanoni** (2020) Systems metabolomics: from metabolomic snapshots to design principles. *Curr Opin Biotechnol.* 2020 Jun;63:190-199. doi: 10.1016/j.copbio.2020.02.013. Epub 2020 Apr 8.
- P26. R. Tisi, V. Gaponenko, M. Vanoni, **E. Sacco** (2020) Natural Products Attenuating Biosynthesis, Processing, and Activity of Ras Oncoproteins: State of the Art and Future Perspectives. *Biomolecules.* 2020 Nov 10;10(11):1535. doi: 10.3390/biom10111535.
- P27. V. Pasquale, G. Ducci, G. Campioni, A. Ventrici, C. Assalini, S. Busti, **M. Vanoni**, R. Vago, **E. Sacco** (2020) Profiling and Targeting of Energy and Redox Metabolism in Grade 2 Bladder Cancer Cells with Different Invasiveness Properties. *Cells.* 2020 Dec 11;9(12):2669. doi: 10.3390/cells9122669.
- P28. C. Raggi, M. L. Taddei, **E. Sacco**, N. Navari, M. Correnti, B. Piombanti, M. Pastore, J. Jorio, G. Lori, M. Lewinska, J.B. Andersen, M. Ramazzotti, I. Orlandi, P. Chiarugi, F. Marra (2021) Mitochondrial oxidative metabolism contributes to a cancer stem cell phenotype in cholangiocarcinoma *J Hepatol.* 2021 Jun;74(6):1373-1385. doi: 10.1016/j.jhep.2020.12.031. Epub 2021 Jan 21. PMID: 33484774.
- P29. R. Tisi, M. Spinelli, A. Palmioli, C. Airoidi, P. Cazzaniga, D. Besozzi, M.S. Nobile, E. Mazzoleni, S. Arnhold, L. De Gioia, R. Grandori, F. Peri, M. Vanoni, **E. Sacco** (2021) The multi-level mechanism of action of a pan-Ras inhibitor explains its antiproliferative activity on Cetuximab-resistant cancer cells *Frontiers in Molecular Biosciences, section Molecular Diagnostics and Therapeutics.* *Front Mol Biosci.* 2021 Feb 17;8:625979. doi: 10.3389/fmolb.2021.625979. PMID: 33681292; PMCID: PMC7925909.
- P30. A. D'Aloia, E. Arrigoni, B. Costa, G. Berruti, E. Martegani, E. Sacco, M. Ceriani (2021) RalGPS2 Interacts with Akt and PDK1 Promoting Tunneling Nanotubes Formation in Bladder Cancer and Kidney Cells Microenvironment. *Cancers (Basel).* 2021 Dec 16;13(24):6330. doi: 10.3390/cancers13246330. PMID: 34944949; PMCID: PMC8699646.
- P31. A. Sforza, V. Vigorelli, E. Rurali, G. Perrucci, E. Gambini, M. Arici, R. Rinaldi, P. Fiorina, A. Barbuti, A. Raucci, E. Sacco, M. Rocchetti, G. Pompilio, S. Genovese & M.C. Vinci (2022) Liraglutide Preserves CD34+ Stem Cells from Dysfunction Induced by High Glucose Exposure *Cardiovascular Diabetology* 21(1):51. doi: 10.1186/s12933-022-01486-9. PMID: 35397526; PMCID: PMC8994898.
- P32. G. Campioni, V. Pasquale, S. Busti, G. Ducci, **E. Sacco**, M. Vanoni (2022) An Optimized Workflow for the Analysis of Metabolic Fluxes in Cancer Spheroids Using Seahorse Technology. *Cells.* 11(5):866. doi: 10.3390/cells11050866. PMID: 35269488; PMCID: PMC8909358.
- P33. A. D'Aloia, M. Ceriani, R. Tisi, S. Stucchi, **E. Sacco***, B. Costa* (2022) Cannabidiol Antiproliferative Effect in Triple-Negative Breast Cancer MDA-MB-231 Cells Is Modulated by Its Physical State and by IGF-1. *Int J Mol Sci.* 23(13):7145. doi: 10.3390/ijms23137145. PMID: 35806150; PMCID: PMC9266539. *co-last authors