CURRICULUM VITAE

PERSONAL INFORMATION

Name: Metello Surname: Innocenti Place of birth: Milan (Italy)

e-mail: metello.innocenti@unimib.it

Languages: Italian (mother tongue), English (C2), French (B2), German (B1)

EDUCATION AND TRAINING

Dec. 12 - Jan. 13: Laboratory Animal Science course (Utrecht University, NL)

Dec. 03 - Sept. 05: AIRC Senior post-doctoral fellow (FIRC Institute of Molecular Oncology, IT)

Nov. 99 - Nov. 03: EIO post-doctoral fellow (European Institute of Oncology, IT)

Oct. 96 - Nov. 99: Ph.D. studentship (University of Milan, IT)

Feb. 96 - Sept. 96: Graduate training fellow (University of Milan, IT)

Nov. 90 - Nov. 95: BSc/MSc in Molecular and Cellular Biology, University of Milan (Milan, IT)

QUALIFICATIONS

Nov. 24: National scientific qualification to function as full professor in Italy (05/E1 Biochemistry)

June. 23: National scientific qualification to function as associate professor in Italy (05/E1 Biochemistry)

Dec. 20: National scientific qualification to function as associate professor in Italy (05/E2 Molecular Biology)

Dec. 20: National scientific qualification to function as associate professor in Italy (05/F1 Applied Biology)

Jan. 13: Laboratory Animal Science Certificate (European Directive 2010/63/EU) - Dutch Art. 9-certified researcher (Utrecht University, NL)

Jan. 00: PhD in Molecular and Cellular Biology (University of Milan, IT)

Jan. 96: BSc/MSc in Molecular and Cellular Biology (University of Milan, IT)

POSITIONS

Nov. 22 - present: Assistant professor, Department of Biotechnology and Biosciences (University of Milano-Bicocca, IT)

Oct. 19 - Oct. 22: Visiting scientist (Heidelberg University Biochemistry Center, DE), reviews editor of FEBS Letters

May 09 - Dec. 17: Tenured Group Leader (The Netherlands Cancer Institute, NL)

Oct. 05 - Apr. 09: Independent Research Group Leader (Goethe University Frankfurt, DE)

TEACHING EXPERIENCE AND OTHER ACADEMIC ACTIVITIES

<u>Teaching experience</u>: Lecturer at the University of Milano-Bicocca (since 2023), Guest Lecturer in Molecular Cell Biology at the University of Leiden (2014 - 2017), Lecturer in Biochemistry at the Frankfurt Medical School (2006 - 2009), and Guest Lecturer in Molecular Oncology at the European School of Molecular Medicine (2003 - 2005).

<u>Conducted courses</u>: Advanced cellular models in preclinical research and personalized medicine at the University of Milano-Bicocca (since 2023), Biochemistry laboratory at the University of Milano-Bicocca (2022), Immunology laboratory at the University of Milano-Bicocca (since 2023), Advanced cellular models in preclinical research and personalized medicine laboratory at the University of Milano-Bicocca (since 2023), Signal transduction and cell migration in the Master's program "Molecular Cell Biology" at the University of Leiden (frontal lectures and exams), biochemistry for undergraduate students at the Frankfurt Medical School (frontal lectures, seminars and exams), signal transduction and cell migration in the PhD program "Molecular Oncology" at the European School of Molecular Medicine (seminars).

<u>Supervision of Doctoral and Diploma candidates</u>: Supervisor and (co-)promotor of eight PhD students [Maria Rita Chelazzi (2024-2026); Silke Gerboth (2004-2006), Debora Mascheroni (2006 - 2010), Petra Beli (2006 - 2010), Magda Galovic (2007 - 2011), Tadamoto Isogai (2010 - 2015), Daniela Leyton-Puig (2011 - 2016), Katarzina Kedziora (2011 - 2016)]. Supervisor and (co-)promotor of six Master students [Yvonne Oligschläger (2011), Nuria Solia-Tapias (2012), Bas Pilzecker (2013), Benjamin Verhoef (2013),

Valentina Gomez (2015), Georgina Zambrano-Munoz (2016)]. Supervisor and (co-)promotor of three undergraduate students [Onur Temocin (2011), Elena Nikonova (2013), Priscilla Natalia (2014)]. Supervisor of three post-doctoral fellows [Dalu Xu (2005 - 2009), Zhen Liu (2009 - 2012), Andrew Campbell (2012)].

<u>Science publishing activities</u>: Member of the Editorial Board of *Scientific Reports* (since 2016), member of the Topics Board of International Journal of *Molecular Science* (since 2020), reviews editor for *FEBS Letters* (2019 - 2022), member of the Editorial Board of *Chinese Journal of Biology* (2014 - 2016), Guest Editor for a Special Issue on "Pathophysiology of Formin Proteins: From Single Molecules to Model Organisms and Human Diseases" (International Journal of *Molecular Science*, 2023).

<u>Peer-reviewing activities</u>: Reviewer for Nature Communications, Science Signaling, The EMBO Journal, Journal of Cell Biology, Journal of Cell Science, Journal of Biological Chemistry, Cellular and Molecular Life Sciences, Molecular and Cellular Biology, Molecular Biology of the Cell, Scientific Reports, Experimental Cell Research, Journal of Neuroscience, International Journal of Cell Biology, Eukaryotic cell, Cells, FEBS Letters, PLOS Biology, PLOS One, Oncogene, Carcinogenesis, Biomaterials, Review Commons, Biosciences, Cells, Frontiers Oncology, *etc.*.

Grant reviewer for the Wellcome Trust Foundation, Human Frontier Science Program Organization, Deutsche Forschungsgemeinschaft (DFG), Wilhelm Sander-Stiftung, Association for International Cancer Research (AICR UK), Italian Association for Cancer Research (AIRC), Austrian Science Fund (FWF), Dutch Cancer Society (KWF), and Natural Sciences and Engineering Research Council of Canada (NSERC).

<u>Organizing activities</u>: Organizer of the Oncology Graduate School Amsterdam (OOA) course "Cytoskeleton in the control of cell migration" (March 4-15, 2013). Host of (inter)national speakers at the Frankfurt Medical School, Leiden University and Netherlands Cancer Institute. Participation in the outreach program of the FIRC Institute of Molecular Oncology as host of talented high-school students.

<u>Programme committees</u>: PhD steering committee member at the Netherlands Cancer Institute (2010 - 2017), PhD committee member at the Free University Amsterdam (2016 - 2017), the Leiden University (2014 - 2016), and the Goethe University (2009 - 2010). Validated expert at the European Commission/Research and Innovation (Horizon 2020) (Expert ID: EX2017D314225).

<u>Membership in scientific societies</u>: Member of the Dutch Society for Cell Biology (2009 - 2017), member of the Cancer Genomics Centre NL (2010 - 2015), member of the Cluster of excellence Frankfurt Macromolecular Complexes (2008 - 2009), member of the Centre for Membrane Proteomics (CMP) Frankfurt (2006 - 2009), member of the German Society for Cell Biology (2006 - 2008), member of the Italian Association for Cellular and Developmental Biology (2000 - 2005).

HONORS AND AWARDS

- 2012, Selected as ERC Consolidator Grant awardee (below financial cutoff).
- 2010, Selected as Cancer Genomics Centre NL Investigator.
- 2008, Selected as Cluster of excellence Frankfurt Macromolecular Complexes Adjunct Investigator.
- 2006, Elected as member of the Centre for Membrane Proteomics Frankfurt.
- 2003, Senior post-doctoral fellowship from the Italian Association for Cancer Research.
- 1999, Post-doctoral fellowship from the European Oncology Foundation.
- 1996, PhD studentship from the Italian Ministry of Research and Education.

MAJOR EXTRAMURAL FUNDS AS PRINCIPAL INVESTIGATOR

<u>Main applicant</u>: Cariplo-Telethon Foundation (2023-2025, 250.000 Euro), Cancer Genomics Centre Netherlands Installation Grant (2010 - 2015, 1.250.000 euros), Cluster of Excellence Frankfurt Macromolecular Complexes (CEF-MC) Adjunct Investigator Grant (2008 - 2009, 200.000 euros), Deutsche Forschungsgemeinschaft (DFG) Research Grant (2009, 300.000 euros, declined owing to relocation to the Netherlands).

<u>Co-applicant</u>: Heal Italia (2023-205, 50.000 Euro), Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) (2011 - 2016, 815.168 euros to K. Jalink), Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) groot (2010 - 2014, 1.500.000 euros to R. Wolthuis), Human Frontiers Long-Term Fellowship (2006 - 2009 to D. Xu), DAAD fellowship (2007 - 2009 to P. Beli).

INVITED SEMINARS AND TALKS

EMBO/FEBS Workshop on Frontiers in Cytoskeleton Research, Gosau (Austria), 2003: "Abi1 is an essential component of a WAVE2-signaling complex mediating Rac-dependent actin remodeling".

Universita' dell'Insubria, Busto Arsizio (Italy), 2004: "Abi1 regulates different Arp2/3 complex-based processes".

Universita' degli Studi di Milano, Milan (Italy), 2004: "Abi1 regulates different Arp2/3 complex-based processes".

San Raffaele Scientific Institute, Milan (Italy), 2004: "Abi1 coordinates different Arp2/3 complex-based processes".

Friedrich Schiller University Jena, Jena (Germany), 2004: "Regulation of Arp2/3 complex activity in cell migration and endocytosis".

University of Münster, Münster (Germany), 2004: "Regulation of Arp2/3 complex activity in cell migration and endocytosis".

Goethe University Frankfurt, Frankfurt (Germany), 2005: "Regulation of Arp2/3 complex activity in cell migration and endocytosis".

EMBO Workshop on Signals and Mechanics in Directed Cell Migration, Heidelberg (Germany), 2006: "The relative levels of Arp2/3 and Drf3 nucleation activity determine the lamellipodial-filopodial selection".

The 7th SACR-ECF meeting, "The cytoskeleton: regulation and motility", Stockholm (Sweden), 2008: "WAVE and Arp2/3 jointly inhibit filopodium formation by entering into a complex with mDia2".

The Netherlands Cancer Institute, Amsterdam (The Netherlands), 2008: "Actin dynamics in control of cell migration and endocytosis".

Ghent University, Ghent (Belgium), 2009: "Actin dynamics in control of cell migration and endocytosis".

ESF-EMBO Symposium Emergent Properties of the Cytoskeleton: Molecules to Cells, San Feliu (Spain), 2010: "Role of mDia2 in filopodium formation as revealed by biochemistry".

Institut Curie, Paris (France), 2010: "Regulation of actin dynamics during clathrin-mediated endocytosis". **CGC-CBG International meeting 2010** "Molecular mechanisms in cancer", Amsterdam (The Netherlands), 2010: "Role of mDia2 in filopodium formation as revealed by biochemistry".

University of Münster, Münster (Germany), 2011: "Role of the N-WASP-CK2 complex in clathrin-mediated endocytosis".

Philipps University of Marburg, Marburg (Germany), 2011: "Role of the N-WASP-CK2 complex in clathrin-mediated endocytosis".

Utrecht University, Utrecht (The Netherlands), 2012: "Interaction maps uncovers new conformation-specific functions for mDia2".

CGC International Meeting 2012, Rotterdam (The Netherlands), 2012: "Interaction maps uncovers new conformation-specific functions for mDia2".

AMOLF, Amsterdam (The Netherlands), 2014: "Cooperation between mDia1 and Arp2/3 complex controls membrane ruffling and cell migration".

EMBO workshop on A Systems-Level View of Cytoskeletal Function, Stockholm (Sweden), 2014: "Cooperation between mDia1 and Arp2/3 complex controls membrane ruffling and cell migration".

Technical University Delft, Delft (The Netherlands), 2015: "Cooperation between mDia1 and Arp2/3 complex controls membrane ruffling and cell migration".

Telethon Institute of Genetics and Medicine (TIGEM), Naples (Italy), 2015: "Actin nucleators: from cell morphogenesis to disease".

Universita' degli Studi di Milano, Milan (Italy), 2015: "Actin in control of cell migration and endocytosis". **European Cytoskeletal Forum - Cell Adhesion and Migration**, Cambridge (United Kingdom), 2016: "Knockout of the Arp2/3 complex in skin epidermis alters Nrf2 activity and causes psoriasis".

Building the Cell 2016, Paris (France), 2016: "Knockout of the Arp2/3 complex in skin epidermis alters Nrf2 activity and causes a psoriasis-like disease".

Leiden University Medical Centre, (The Netherlands), 2016: "Actin nucleators in control of cell migration and endocytosis".

Institute for Integrative Biology of the Cell (I2BC), Gif-sur-Yvette (France), 2016: "Arp2/3 and formins in health and disease".

Institut Curie, Paris (France), 2017: "Multiscale analysis of the Arp2/3 complex and formins in health and disease".

Gustave Roussy, Paris (France), 2017: "Multiscale analysis of the Arp2/3 complex and formins: from basic biology to breast cancer metastasis".

Hubrecht Organoid Technology Centre (HUB), Utrecht (The Netherlands), 2017: "Multiscale analysis of the Arp2/3 complex and formins in health and disease".

IRCCS Ospedale San Raffaele (HSR), Milan (Italy), 2021: "Multiscale analysis of actin-based processes in health and disease".

Universita' Milano Bicocca, Milan (Italy), 2022: "Multiscale analysis of the Arp2/3 complex and formins: from basic biology to cancer and back".

PEER-REVIEWED PUBLICATIONS

36. TGF-β Signaling Loop in Pancreatic Ductal Adenocarcinoma Activates Fibroblasts and Increases Tumor Cell Aggressiveness.

di Miceli N, Baioni C, Barbieri L, Danielli D, Sala E, Salvioni L, Garbujo S, Colombo M, Prosperi D, **Innocenti M***, Fiandra L.

Cancers (Basel). 2024 Nov 1;16(21):3705. (* co-corresponding author).

35. Multiplexed imaging to reveal tissue dendritic cell spatial localisation and function.

Rocca G, Galli M, Celant A, Stucchi G, Marongiu L, Cozzi S, Innocenti M*, Granucci F.

FEBS Lett. 2024 Jul 5. (* co-corresponding author).

34. Aberrant cortex contractions impact mammalian oocyte quality.

Nikalayevich E, Letort G, de Labbey G, Todisco E, Shihabi A, Turlier H, Voituriez R, Yahiatene M, Pollet-Villard X, Innocenti M, Schuh M, Terret ME, Verlhac MH.

Dev Cell. 2024 Apr 8;59(7):841-852.e7.

33. Investigating Mammalian Formins with SMIFH2 Fifteen Years in: Novel Targets and Unexpected Biology.

Innocenti M.

Int J Mol Sci 2023 May 21;24(10):9058.

32. Advanced Cell Culture Models Illuminate the Interplay between Mammary Tumor Cells and Activated Fibroblasts.

Del Nero M, Colombo A, Garbujo S, Baioni C, Barbieri L, **Innocenti M**, Prosperi D, Colombo M, Fiandra L. Cancers (Basel). 2023 Apr 26;15(9):2498.

31. A pro-tumorigenic mDia2-MIRO1 axis controls mitochondrial positioning and function in cancer-associated fibroblasts.

Cangkrama M, Liu H, Whipman J, Zubair M, Matsushita M, Di Filippo M, Kopf M, Innocenti M*, Werner S. Cancer Res. 2022 Aug 23:CAN-22-0162 (* co-corresponding author).

See also accompanying journal's cover page.

30. mDia1 assembles a linear actin coat at membrane invaginations to drive *Listeria monocytogenes* cell-to-cell spreading.

Dhanda AS, A. Vogl W, Ness F, Innocenti M* and Guttman JA.

mBio 2021 Dec 21;12(6):e0293921 (* co-corresponding author).

29. mTORC1 and mTORC2 converge on the Arp2/3 complex to promote Kras^{G12D}-induced acinar-to-ductal metaplasia and early pancreatic carcinogenesis.

Zhao Y, Schoeps B, Yao D, Zhang Z, Schuck K, Tissen V, Jäger C, Schlitter AM, van der Kammen R, Ludwig C, D'Haese JG, Raulefs S, Maeritz N, Shen S, Zou X, Krüger A, Kleeff J, Michalski CW, Friess H, Innocenti M, Kong B.

Gastroenterology 2021 Apr;160(5):1755-1770.e17.

28. A paracrine activin A-mDia2 axis promotes squamous carcinogenesis via fibroblast reprogramming. Cangkrama M, Wietecha M, Mathis N, Okumura R, Ferrarese L, Al-Nuaimi D, Antsiferova M, Dummer R, Innocenti M, Werner S.

EMBO Mol Med. 2020 Apr 7;12(4):e11466.

See also News and Views entitled "Cancer-associated fibroblasts: activin A adds another string to their bow".

27. The chloride intracellular channel protein CLIC4 inhibits filopodium formation induced by constitutively active mutants of formin mDia2.

Argenzio E, Innocenti M.

FEBS Lett. 2020 Jun;594(11):1750-1758.

26. Profilin 1 binding couples chloride intracellular channel protein CLIC4 to RhoA–mDia2 signaling and filopodium formation.

Argenzio E, Klarenbeek J, Kedziora KM, Nahidiazar L, Isogai T, Jalink K, Moolenaar WH, Innocenti M.

J Biol Chem. 2018 Dec 14;293(50):19161-19176.

See also accompanying journal's cover page.

25. New insights into the formation and the function of lamellipodia and ruffles in mesenchymal cells. **Innocenti M.**

Cell Adh Migr. 2018 Mar 7:1-41.

24. Knockout of the Arp2/3 complex in epidermis causes a psoriasis-like disease hallmarked by hyperactivation of transcription factor Nrf2.

van der Kammen R, Song JY, de Rink I, Janssen H, Madonna S, Scarponi C, Albanesi C, Kerkhoven R, Innocenti M.

Development. 2017 Dec 15;144(24):4588-4603.

See also IN THIS ISSUE entitled "Branched actin keeps Nrf2 in check in the skin".

23. Flat clathrin lattices are dynamic actin-controlled hubs for clathrin-mediated endocytosis and signalling of specific receptors.

Leyton-Puig D, Isogai T, Argenzio E, van der Broek B, Klarenbeek J, Janssen H, Jalink K, **Innocenti M.** Nat Commun. 2017 Jul 13;8:16068.

- 22. Quantitative proteomics illuminates a functional interaction between mDia2 and the proteasome. Isogai T, van der Kammen R, Goerdayal SS, Argenzio E, Altelaar AFM, **Innocenti M.** J Proteome Res. 2016 Dec 2;15(12):4624-4637.
- 21. New nuclear and perinuclear functions of formins.

Isogai T, Innocenti M.

Biochem Soc Trans. 2016 Dec 15;44(6):1701-1708.

20. PFA fixation enables artifact-free super-resolution imaging of the actin cytoskeleton and associated proteins.

Leyton-Puig D, Kedziora KM, Isogai T, van der Broek B, Jalink K, Innocenti M.

Biol Open. 2016 Jul 15;5(7):1001-9.

See also accompanying journal's cover page.

19. Invadosomes - shaping actin networks to follow mechanical cues.

Kedziora KM, Isogai T, Jalink K, Innocenti M.

Front Biosci. (Landmark Ed) 2016 Jun 1;21:1092-11.

18. Rapid remodeling of invadosomes by Gi-coupled receptors: dissecting the role of Rho GTPases. Kedziora KM, Leyton-Puig D, Argenzio E, Boumeester AJ, van Butselaar B, Yin T, Wu YI, van Leeuwen FN, **Innocenti M**, Jalink K, Moolenaar WH.

J Biol Chem. 2016 Feb 26;291(9):4323-33.

See also accompanying journal's cover page.

17. Initiation of lamellipodia and ruffles involves cooperation between mDia1 and the Arp2/3 complex. Isogai T, van der Kammen R, Leyton-Puig D, Kedziora KM, Jalink K, **Innocenti M**.

J Cell Sci. 2015 Oct 15;128(20):3796-810.

See also IN THIS ISSUE entitled "Arp2/3 and mDia1 cooperate to make a ruffle".

16. SMIFH2 has effects on Formins and p53 that perturb the cell cytoskeleton.

Isogai T, van der Kammen R, Innocenti M.

Sci Rep. 2015 Apr 30;5:9802.

15. Proteomic analyses uncover a new function and mode of action for mouse homolog of Diaphanous 2 (mDia2)

Isogai T, van der Kammen R, Goerdayal SS, Heck AJ, Altelaar AF, Innocenti M.

Mol Cell Proteomics. 2015 Apr;14(4):1064-78.

14. Interplay between N-WASP and CK2 optimizes clathrin-mediated endocytosis of EGFR.

Galovic M, Xu D, Areces LB, van der Kammen R, Innocenti M.

J Cell Sci. 2011 Jun 15;124(Pt 12):2001-12.

WAVE and Arp2/3 jointly inhibit filopodium formation by entering into a complex with mDia2.

Beli P, Mascheroni D, Xu D, Innocenti M.

Nat Cell Biol. 2008 Jul;10(7):849-57.

This paper is part of the prestigious Nature Milestones Cytoskeleton (www.nature.com/milestones/milecyto).

12. Abi1 regulates the activity of N-WASP and WAVE in distinct actin-based processes.

Innocenti M, Gerboth S, Rottner K, Lai FP, Hertzog M, Stradal TE, Frittoli E, Didry D, Polo S, Disanza A, Benesch S, Di Fiore PP, Carlier MF, Scita G.

Nat Cell Biol. 2005 Oct;7(10):969-76.

11. WASP-related proteins, Abi1 and Ena/VASP are required for Listeria invasion induced by the Met receptor.

Bierne H, Miki H, Innocenti M, Scita G, Gertler FB, Takenawa T, Cossart P. J Cell Sci. 2005 Apr 1;118(Pt 7):1537-47.

- 10. Role of phosphoinositide 3-kinase regulatory isoforms in development and actin rearrangement. Brachmann SM, Yballe CM, **Innocenti M**, Deane JA, Fruman DA, Thomas SM, Cantley LC. Mol Cell Biol. 2005 Apr;25(7):2593-606.
- 9. Regulation of actin dynamics by WASP and WAVE family proteins. Stradal TE, Rottner K, Disanza A, Confalonieri S, **Innocenti M**, Scita G. Trends Cell Biol. 2004 Jun;14(6):303-11.
- 8. Abi1 is essential for the formation and activation of a WAVE2 signalling complex. **Innocenti M**, Zucconi A, Disanza A, Frittoli E, Areces LB, Steffen A, Stradal TE, Di Fiore PP, Carlier MF, Scita G.

Nat Cell Biol. 2004 Apr;6(4):319-27.

See also News and Views entitled "Solving the WAVE function".

- 7. Sra-1 and Nap1 link Rac to actin assembly driving lamellipodia formation. Steffen A, Rottner K, Ehinger J, **Innocenti M**, Scita G, Wehland J, Stradal TE. EMBO J. 2004 Feb 25;23(4):749-59.
- 6. Phosphoinositide 3-kinase activates Rac by entering in a complex with Eps8, Abi1, and Sos-1. **Innocenti M**, Frittoli E, Ponzanelli I, Falck JR, Brachmann SM, Di Fiore PP, Scita G. J Cell Biol. 2003 Jan 6;160(1):17-23.
- 5. Mechanisms through which Sos-1 coordinates the activation of Ras and Rac. **Innocenti M**, Tenca P, Frittoli E, Faretta M, Tocchetti A, Di Fiore PP, Scita G. J Cell Biol. 2002 Jan 7;156(1):125-36. See also the dedicated review entitled "The two hats of SOS" (Science, 2002, 36).
- 4. An effector region in Eps8 is responsible for the activation of the Rac-specific GEF activity of Sos-1 and for the proper localization of the Rac-based actin-polymerizing machine.

 Scita G, Tenca P, Areces LB, Tocchetti A, Frittoli E, Giardina G, Ponzanelli I, Sini P, Innocenti M, Di Fiore

J Cell Biol. 2001 Sep 3;154(5):1031-44.

- 3. Cloning and characterization of mouse UBPy, a deubiquitinating enzyme that interacts with the ras guanine nucleotide exchange factor CDC25(Mm)/Ras-GRF1.

 Gnesutta N, Ceriani M, Innocenti M, Mauri I, Zippel R, Sturani E, Borgonovo B, Berruti G, Martegani E. J Biol Chem. 2001 Oct 19;276(42):39448-54.
- 2. Signaling from Ras to Rac and beyond: not just a matter of GEFs. Scita G, Tenca P, Frittoli E, Tocchetti A, **Innocenti M**, Giardina G, Di Fiore PP. EMBO J. 2000 Jun 1;19(11):2393-8.
- 1. CDC25(Mm)/Ras-GRF1 regulates both Ras and Rac signaling pathways. **Innocenti M**, Zippel R, Brambilla R, Sturani E. FEBS Lett. 1999 Oct 29;460(2):357-62.