

Curriculum vitae

Name: Stefania Scala, M.D., Ph.D.
Date & Place of Birth: April 18, 1963, Naples, Italy
Citizenship: Italian
Education: 1988 M.D. Medical School "Federico II", Naples; 1991 Oncology Specialist Medical School "Federico II", Naples, 1991 General Fellow and Fogarty Fellow. National Cancer Institute, Bethesda USA, 2000 Ph.D in Cellular and Molecular Biology and Pathology, Naples, Italy

A. Main domain of research

The main domain of the research is studying cancer microenvironment to identify and validate new molecular target in cancer. Chemokine receptors, mainly CXCR4 and CXCR7 play a central role in cancer development and metastatic disseminations of multiple solid and hematopoietic neoplasias. CXCR4 and CXCR7 demonstrated to be prognostic marker and predictive of response to drugs in colorectal and renal cancer. From 2009 to present, Stefania Scala direct the translational Research Section in the Molecular Immunology and Immunoregulation at the National Cancer Institute, "Pascale", Naples.

B. Positions and Honors

Professional experience:

1990-1996 Postdoctoral fellow, General Fellow and Fogarty Fellow at the Medicine Branch, NIH, Bethesda, MD, USA; 1996- 1999 PhD in Biology and Pathology Cellular and Molecular, Naples, ITALY
1999-2002 Senior Reseracher "Biogem" scarl, Ariano Irpino, (AV)
2002-2009 Medical Staff, Immunology
2009-today Group Leader, Immunology, National Cancer Institute "G. Pascale", Naples
Awards: 1990-1994 General Fellow, Medicine Branch NCI, NIH, Bethesda, MD, 1994-1995 Fogarty Fellow Medicine Branch NCI, NIH, Bethesda, MD, 1999-2002 Senior Researcher "Biogem", Ariano Irpino (AV)

C. 5-years Publications:

1. D'Alterio C, Nasti G, Polimeno M, Ottaiano A, Conson M, Circelli L, Botti G, Scognamiglio G, Santagata S, De Divitiis C, Nappi C, Napolitano M, Tatangelo F, Pacelli R, Izzo F, Vuttariello E, Botti G and, Scala S. CXCR4-CXCL12-CXCR7, TLR2-4, PD-1/PD-L1 IN COLORECTAL-LIVER METASTASES FROM NEOADJUVANT TREATED PATIENTS. *Oncoimmunology*. In press
2. Di Maro S, Trotta AM, Brancaccio D, Di Leva FS, La Pietra V, Ierano C, Napolitano M, Portella L, D'Alterio C, Siciliano RA, Sementa D, Tomassi S, Carotenuto A, Novellino E, **Scala S**, Marinelli L. Exploring the N-terminal region of C-X-C motif chemokine 12 (CXCL12): Identification of plasma-stable cyclic peptides as novel, potent C-X-C chemokine receptor type 4 (CXCR4) antagonists. *J Med Chem*. 2016 Aug 29. PMID:27571038
3. Gargiulo P, Della Pepa C, Berardi S, Califano D, **Scala S**, Buonaguro L, Ciliberto G, Brauchli P, Pignata S. Tumor genotype and immune microenvironment in POLE-ultramutated and MSI-hypermuted Endometrial Cancers: New candidates for checkpoint blockade immunotherapy? *Cancer Treat Rev*. 2016 Jul;48:61-8. doi: 10.1016/j.ctrv.2016.06.008.
4. Scognamiglio G, De Chiara A, Di Bonito M, Tatangelo F, Losito NS, Anniciello A, De Cecio R, D'Alterio C, **Scala S**, Cantile M, Botti G. Variability in Immunohistochemical Detection of Programmed Death Ligand 1 (PD-L1) in Cancer Tissue Types.
5. Ieranò C, Portella L, Lusa S, Salzano G, D'Alterio C, Napolitano M, Buoncervello M, Macchia D, Spada M, Barbieri A, Luciano A, Barone MV, Gabriele L, Caraglia M, Arra C, De Rosa G, **Scala S**. CXCR4-antagonist Peptide R-liposomes for combined therapy against lung metastasis. *Nanoscale*. 2016 Mar 31;8(14):7562-71. doi: 10.1039/c5nr06335c.
6. Mercurio, L, Ajmone-Cat MA, Cecchetti S, Ricci A, Bozzuto G, Molinari A, Manni I, Pollo B, **Scala S**, Carpinelli G, Minghetti L. Targeting CXCR4 by a selective peptide antagonist modulates tumor microenvironment and microglia reactivity in a human glioblastoma model. *J Exp Clin Cancer Res*. 2016 Mar 25;35(1):55. doi: 10.1186/s13046-016-0326-y.

7. Trotta AM, Ottaiano A, Romano C, Nasti G, Nappi A, De Divitiis C, Napolitano M, Zanotta S, Casaretti R, D'Alterio C, Avallone A, Califano D, Iaffaioli RV, **Scala S**. Prospective evaluation of cetuximab-mediated antibody-dependent cell cytotoxicity (ADCC) in metastatic colorectal cancer patients predicts treatment efficacy. *Cancer Immunol Res.* 2016 Jan 27. pii: canimm.0184.2015.
8. Ottaiano A, Nappi A, Tafuto S, Nasti G, De Divitiis C, Romano C, Cassata A, Casaretti R, Silvestro L, Avallone A, Capuozzo M, Capozzi M, Maiolino P, Quagliariello V, **Scala S**, Iaffaioli VR. Diabetes and Body Mass Index Are Associated with Neuropathy and Prognosis in Colon Cancer Patients Treated with Capecitabine and Oxaliplatin Adjuvant Chemotherapy. *Oncology.* 2016 Jan 6 PubMed PMID: 26731722.
9. Fontanella R, Pelagalli A, Nardelli A, D'Alterio C, Ieranò C, Cerchia L, Lucarelli E, **Scala S**, Zannetti A. A novel antagonist of CXCR4 prevents bone marrow-derived mesenchymal stem cell-mediated osteosarcoma and hepatocellular carcinoma cell migration and invasion. *Cancer Lett.* 2016 Jan 1;370(1):100-7. doi:10.1016/j.canlet.2015.10.018. Epub 2015 Oct 27. PubMed PMID: 26517945.
10. Vincenzi M, Accardo A, Costantini S, **Scala S**, Portella L, Trotta A, Ronga L, Guillon J, Leone M, Colonna G, Rossi F, Tesaro D. Intrinsically disordered amphiphilic peptides as potential targets in drug delivery vehicles. *Mol Biosyst.* 2015 Nov;11(11):2925-32. doi: 10.1039/c5mb00358j. PubMed PMID: 26263446.
11. **Scala S**. Molecular Pathways: Targeting the CXCR4-CXCL12 Axis—Untapped Potential in the Tumor Microenvironment. *Clin Cancer Res.* 2015 Oct 1;21(19):4278-85. doi: 10.1158/1078-0432.CCR-14-0914. Epub 2015 Jul 21. PubMed PMID: 26199389.
12. Capozzi M, Caterina I, De Divitiis C, von Arx C, Maiolino P, Tatangelo F, Cavalcanti E, Di Girolamo E, Iaffaioli RV, **Scala S**, Tafuto S; ENETS Center of Excellence Multidisciplinary Group for Neuroendocrine Tumors in Naples (Italy). Everolimus and pancreatic neuroendocrine tumors (PNETs): Activity, resistance and how to overcome it. *Int J Surg.* 2015 Sep;21 Suppl 1:S89-94. doi:10.1016/j.ijisu.2015.06.064. Epub 2015 Jun 27. PubMed PMID: 26123382.
13. Neve Polimeno M, Ierano C, D'Alterio C, Simona Losito N, Napolitano M, Portella L, Scognamiglio G, Tatangelo F, Maria Trotta A, Curley S, Costantini S, Liuzzi R, Izzo F, **Scala S**. CXCR4 expression affects overall survival of HCC patients whereas CXCR7 expression does not. *Cell Mol Immunol.* 2015 Jul;12(4):474-82. doi: 10.1038/cmi.2014.102. Epub 2014 Nov 3. PubMed PMID:25363530; PubMed Central PMCID: PMC4496532.
14. Circelli L, Ramundo V, Marotta V, Sciammarella C, Marciello F, Del Prete M, Sabatino L, Pasquali D, Izzo F, **Scala S**, Colao A, Faggiano A, Colantuoni V; Multidisciplinary Group for NeuroEndocrine Tumours of Naples. Prognostic role of the CDNK1B V109G polymorphism in multiple endocrine neoplasia type 1. *J Cell Mol Med.* 2015 Jul;19(7):1735-41. doi: 10.1111/jcmm.12552. Epub 2015 Mar 30. PubMed PMID: 25824098
15. Vincenzi M, Costantini S, **Scala S**, Tesaro D, Accardo A, Leone M, Colonna G, Guillon J, Portella L, Trotta AM, Ronga L, Rossi F. Conformational ensembles explored dynamically from disordered peptides targeting chemokine receptor CXCR4. *Int J Mol Sci.* 2015 May 28;16(6):12159-73. doi: 10.3390/ijms160612159. PubMed PMID: 26030674; PubMed Central PMCID: PMC4490436.
16. Cioffi M, D'Alterio C, Camerlingo R, Tirino V, Consales C, Riccio A, Ieranò C, Cecere SC, Losito NS, Greggi S, Pignata S, Pirozzi G, **Scala S**. Identification of a distinct population of CD133(+)CXCR4(+) cancer stem cells in ovarian cancer. *Sci Rep.* 2015 May 28;5:10357. doi: 10.1038/srep10357. PubMed PMID: 26020117.
17. Napolitano M, D'Alterio C, Cardone E, Trotta AM, Pecori B, Rega D, Pace U, Scala D, Scognamiglio G, Tatangelo F, Cacciapuoti C, Pacelli R, Delrio P, **Scala S**. Peripheral myeloid-derived suppressor and T regulatory PD-1 positive cells predict response to neoadjuvant short-course radiotherapy in rectal cancer patients. *Oncotarget.* 2015 Apr 10;6(10):8261-70. PubMed PMID: 25823653; PubMed Central PMCID: PMC4480750.
18. D'Alterio C, Avallone A, Tatangelo F, Delrio P, Pecori B, Cella L, Pelella A, D'Armiento FP, Carlomagno C, Bianco F, Silvestro L, Pacelli R, Napolitano M, Iaffaioli RV, **Scala S**. A prognostic model comprising pT stage, N status, and the chemokine receptors CXCR4 and CXCR7 powerfully predicts outcome in neoadjuvant resistant rectal cancer patients. *Int J Cancer.* 2014 Jul 15;135(2):379-90. doi: 10.1002/ijc.28689. Epub 2014 Jan 10. PubMed PMID: 24375277.
19. Costantini S, Raucci R, Colonna G, Mercurio FA, Trotta AM, Paola R, Leone M, Rossi F, Pellegrino C, Castello G, **Scala S**. Peptides targeting chemokine receptor CXCR4: structural behavior and biological binding studies. *J Pept Sci.* 2014 Apr;20(4):270-8. doi: 10.1002/psc.2614. Epub 2014 Jan 28. PubMed PMID: 24474664.
20. Scognamiglio G, Cantile M, **Scala S**, Cecere S, Russo F, Collina F, Marra L, Sabbatino F, Botti G, Franco R. Tissue micro arrays for immunohistochemical detection of inflammatory infiltrates

- in renal cell carcinoma. *Int J Clin Exp Med*. 2014 Apr 15;7(4):1175-9. eCollection 2014. PubMed PMID: 24955204; PubMed Central PMCID: PMC4057883.
21. Scognamiglio G, Cantile M, **Scala S**, Cecere S, Russo F, Collina F, Marra L, Sabbatino F, Botti G, Franco R. Tissue Micro Arrays for immunohistochemical detection of inflammatory infiltrates in renal cell carcinoma. *Int J Clin Exp Pathol*. 2014 Mar 15;7(4):1814-8. eCollection 2014. PubMed PMID: 24817986; PubMed Central PMCID: PMC4014270.
 22. Deriu PL, La Pietra L, Pierotti M, Collazzo R, Paradiso A, Belardelli F, De Paoli P, Nigro A, Lacalamita R, Ferrarini M, Pelicci P, Pierotti M, Roli A, Ciliberto G, **Scala S**, Amadori A, Chiusole D, Musto P, Fusco V, Storto G, De Maria R, Canitano S, Apolone G, Ravelli M, Mazzini E, Amadori D, Bernabini M, Ancarani V, Lombardo C. Accreditation for excellence of cancer research institutes: recommendations from the Italian Network of Comprehensive Cancer Centers. *Tumori*. 2013 Nov-Dec;99(6):293e-8e. doi: 10.1700/1390.15472. PubMed PMID: 24503807.
 23. Polimeno M, Napolitano M, Costantini S, Portella L, Esposito A, Capone F, Guerriero E, Trotta A, Zanotta S, Pucci L, Longo N, Perdonà S, Pignata S, Castello G, **Scala S**. Regulatory T cells, interleukin (IL)-6, IL-8, vascular endothelial growth factor (VEGF), CXCL10, CXCL11, epidermal growth factor (EGF) and hepatocyte growth factor (HGF) as surrogate markers of host immunity in patients with renal cell carcinoma. *BJU Int*. 2013 Sep;112(5):686-96. doi:10.1111/bju.12068. Epub 2013 Mar 15. PubMed PMID: 23495770.
 24. Ieranò C, Santagata S, Napolitano M, Guardia F, Grimaldi A, Antignani E, Botti G, Consales C, Riccio A, Nanayakkara M, Barone MV, Caraglia M, **Scala S**. CXCR4 and CXCR7 transduce through mTOR in human renal cancer cells. *Cell Death Dis*. 2014 Jul 3;5:e1310. doi: 10.1038/cddis.2014.269.
 25. Pacelli R, Conson M, Cella L, Liuzzi R, Troncone G, Iorio V, Solla R, Farella A, **Scala S**, Pagliarulo C, Salvatore M. Radiation therapy following surgery for localized breast cancer: outcome prediction by classical prognostic factors and approximated genetic subtypes. *J Radiat Res*. 2013 Mar 1;54(2):292-8. doi:10.1093/jrr/rrs087. Epub 2012 Sep 26. PubMed PMID: 23019151; PubMed Central PMCID: PMC3589925.
 26. Ierano C, Basseville A, To KK, Zhan Z, Robey RW, Wilkerson J, Bates SE, **Scala S**. Histone deacetylase inhibitors induce CXCR4 mRNA but antagonize CXCR4 migration. *Cancer Biol Ther*. 2013 Feb;14(2):175-83. doi: 10.4161/cbt.22957. Epub 2012 Nov 28. PubMed PMID: 23192271; PubMed Central PMCID: PMC3571999.
 27. Portella L, Vitale R, De Luca S, D'Alterio C, Ieranò C, Napolitano M, Riccio A, Polimeno MN, Monfregola L, Barbieri A, Luciano A, Ciarmiello A, Arra C, Castello G, Amodeo P, **Scala S**. Preclinical development of a novel class of CXCR4 antagonist impairing solid tumors growth and metastases. *PLoS One*. 2013 Sep 13;8(9):e74548. doi: 10.1371/journal.pone.0074548. eCollection 2013. PubMed PMID: 24058588; PubMed Central PMCID: PMC3772838.
 28. Mattei F, Schiavoni G, Sestili P, Spadaro F, Fragale A, Sistigu A, Lucarini V, Spada M, Sanchez M, **Scala S**, Battistini A, Belardelli F, Gabriele L. IRF-8 controls melanoma progression by regulating the cross talk between cancer and immune cells within the tumor microenvironment. *Neoplasia*. 2012 Dec;14(12):1223-35. PubMed PMID: 23308054; PubMed Central PMCID: PMC3540947.
 29. Calemma R, Ottaiano A, Trotta AM, Nasti G, Romano C, Napolitano M, Galati D, Borrelli P, Zanotta S, Cassata A, Castello G, Iaffaioli VR, **Scala S**. Fc gamma receptor IIIa polymorphisms in advanced colorectal cancer patients correlated with response to anti-EGFR antibodies and clinical outcome. *J Transl Med*. 2012 Nov 21;10:232. doi: 10.1186/1479-5876-10-232. PubMed PMID: 23171437; PubMed Central PMCID: PMC3551834.
 30. D'Alterio C, Barbieri A, Portella L, Palma G, Polimeno M, Riccio A, Ieranò C, Franco R, Scognamiglio G, Bryce J, Luciano A, Rea D, Arra C, **Scala S**. Inhibition of stromal CXCR4 impairs development of lung metastases. *Cancer Immunol Immunother*. 2012 Oct;61(10):1713-20. Epub 2012 Mar 8. PubMed PMID: 22399057; PubMed Central PMCID: PMC3448054.
 31. Palladino P, Portella L, Colonna G, Raucci R, Saviano G, Rossi F, Napolitano M, **Scala S**, Castello G, Costantini S. The N-terminal region of CXCL11 as structural template for CXCR3 molecular recognition: synthesis, conformational analysis, and binding studies. *Chem Biol Drug Des*. 2012 Aug;80(2):254-65. Doi:10.1111/j.1747-0285.2012.01397.x. Epub 2012 May 23. PubMed PMID: 22531000.
 32. Franco R, Pirozzi G, **Scala S**, Cantile M, Scognamiglio G, Camerlingo R, Botti G, Rocco G. CXCL12-binding receptors expression in non-small cell lung cancer relates to tumoral microvascular density and CXCR4 positive circulating tumoral cells in lung draining venous blood. *Eur J Cardiothorac Surg*. 2012 Feb;41(2):368-75. doi: 10.1016/j.ejcts.2011.05.009. Epub 2011 Dec 12. PubMed PMID: 21683606.
 33. Tocchetti CG, Ragone G, Coppola C, Rea D, Piscopo G, **Scala S**, De Lorenzo C, Iaffaioli RV, Arra C, Maurea N. Detection, monitoring, and management of trastuzumab-induced left

- ventricular dysfunction: an actual challenge. *Eur J Heart Fail.* 2012 Feb;14(2):130-7. doi: 10.1093/eurjhf/hfr165. Epub 2012 Jan 4. Review. PubMed PMID: 22219501.
34. Ottaiano A, Capuozzo M, Nasti G, Maiolino P, De Angelis V, **Scala S**, Iaffaioli RV. Prediction of response to anti-EGFR antibodies in metastatic colorectal cancer: looking beyond EGFR inhibition. *Front Immunol.* 2013 Jan 7;3:409. doi:10.3389/fimmu.2012.00409. eCollection 2012. PubMed PMID: 23316197; PubMed Central PMCID: PMC3539668.
 35. Di Stasio M, Volpe MG, Colonna G, Nazzaro M, Polimeno M, **Scala S**, Castello G, Costantini S. A possible predictive marker of progression for hepatocellular carcinoma. *Oncol Lett.* 2011 Nov;2(6):1247-1251. Epub 2011 Aug 9. PubMed PMID:22848296; PubMed Central PMCID: PMC3406508.