

Luciana D'Apice

PERSONAL INFORMATION

Birthplace: Vico Equense (Na)
Birthdate: October 12 1972
Marital Status: married, 2 children

EDUCATION

1995 **Degree in Biology** at the “Università degli Studi di Napoli Federico II” Naples, Italy

2001 Biochemistry and Molecular Biology **Ph.D** at the “Università degli Studi di Napoli Federico II” Naples, Italy

Actual position: Researcher (permanent position) at Institute of Protein Biochemistry, National Council of Research, since 2008.

POSTDOCTORAL TRAINING

1996-1999 Institute of Protein Biochemistry, CNR. Immunology laboratory, research for PhD dissertation.

1999-2000 Institute Pasteur, Paris, France, Molecular Immunology Unit, guest in dr. O. Acuto's team.

2001 Università degli Studi Federico II, Naples, pediatry department. Fellowship on “Analisi di linfociti T gliadina-specifici isolati dalla mucosa intestinale e dal sangue venoso di pazienti affetti da celiachia”.

2002-2004 Institute of Protein Biochemistry, CNR. Immunology laboratory, fellowship on the research project “Sistemi di veicolazione antigenica”.

2005-2007 Institute of Protein Biochemistry, CNR. Immunology laboratory, FIRB Fellowship: “Analisi comparata in vitro e in vivo di vaccini ricombinanti innovativi basati su sistemi procariotici di display, proteine di fusione e peptidi bioattivi”.

2007 Institute of Protein Biochemistry, CNR. Immunology laboratory, fellowship on “Analisi della risposta antitumorale specifica per l'antigene Mage3”.

Membership in Scientific Societies:

Italian Society of immunology, Clinical Immunology and allergology (SIICA)

Language: English, French.

Advanced Courses: 1997 Ruggero Ceppellini Advanced School of Immunology

“Cytokines in Immunity” Napoli.

1999 Ruggero Ceppellini Advanced School of Immunology

“L’immunità in patologia umana” Napoli.

1999 Ruggero Ceppellini Advanced School of Immunology

“Dendritic cell physiology” Postano (Sa).

2002 FEBS International Summer School on Immunology: “The immune system: genes, receptors and regulation” Ionian Village, Grecia.

2008 Ruggero Ceppellini Advanced School of Immunology

“Tumor Immunology” Sorrento (Na)

SCIENTIFIC PRODUCTION

R. SARTORIUS, L. D’APICE, M. TROVATO, F. CUCCARO, V. COSTA, M. G. DE LEO, V. M. MARZULLO, C. BIONDO, S. D’AURIA, M. A. DE MATTEIS, A. CICCODICOLA, P. DE BERARDINIS. (2015)

Antigen delivery by Filamentous bacteriophage fd displaying an anti-DEC-205 single-chain variable fragment confers adjuvanticity by triggering a TLR9-mediated immune response. EMBO Mol Med. 2015 Apr 17.

Patent n. RM2014A000632 “Varianti del recettore delle cellule T e loro uso nella terapia tumorale”

Authors: P. DE BERARDINIS, L. D’APICE, U. ORESTE

D’APICE L, COSTA V, VALENTE C, TROVATO M, PAGANI A, MANERA S, REGOLO L, ZAMBELLI A, CICCODICOLA A, DE BERARDINIS P.(2013)

Analysis of SEMA6B gene expression in breast cancer: identification of a new isoform. Biochim Biophys Acta. 2013 Oct;1830(10):4543-53. doi: 10.1016/j.bbagen.2013.05.003. Epub 2013 May 9.

JAWORSKI JP, KREBS S, TROVATO M, KOVARIK DN, BROWER Z, SUTTON WF, WAAGMEESTER G, SARTORIUS R, D’APICE L, CAIVANO A, DORIA-ROSE NA, MALHERBE D, MONTEFIORI D, BARNETT S, DE BERARDINIS P, HAIGWOOD NL, (2012)

Co-immunization with Multimeric Scaffolds and DNA Rapidly Induces Potent Autologous HIV-1 Neutralizing Antibodies and CD8+ T Cells PLoS One. 2012;7(2):e31464

COSTA V, ANGELINI C, **D'APICE L**, MUTARELLI M, CASAMASSIMI A, SOMMESE L, GALLO MA, APRILE M, ESPOSITO R, LEONE L, DONIZZETTI A, CRISPI S, RIENZO M, SARUBBI B, CALABRO' R, PICARDI M, SALVATORE P, INFANTE T, DE BERARDINIS P, NAPOLI C, CICCODICOLA A. (2011) Massive-scale RNA-Seq analysis of non ribosomal transcriptome in human trisomy 21. PLoS One. Apr 20;6(4):e18493.

SARTORIUS R, BETTUA C, **D'APICE L**, CAIVANO A, TROVATO M, RUSSO D, ZANONI I, GRANUCCI F, MASCOLO D, BARBA P, DEL POZZO G, DE BERARDINIS P. (2011) Vaccination with filamentous bacteriophages targeting DEC-205 induces DC maturation and potent anti-tumor T-cell responses in the absence of adjuvants. Eur J Immunol. 2011 Sep;41(9):2573-84. doi: 10.1002/eji.201141526. Epub 2011 Aug 18.

CAIVANO A, DORIA-ROSE NA, BUELOW B, SARTORIUS R, TROVATO M, **D'APICE L**, DOMINGO GJ, SUTTON WF, HAIGWOODNL, DE BERARDINIS P. HIV-1 Gag p17 presented as virus-like particles on the E2 scaffold from Geobacillus stearothermophilus induces sustained humoral and cellular immune responses in the absence of IFN γ production by CD4+ T cells. Virology. 2010 Nov 25;407(2):296-305. Epub 2010 Sep 20.

DEL POZZO G, MASCOLO D, SARTORIUS R, CITRO A, BARBA P, **D'APICE L**, DE BERARDINIS P. Triggering DTH and CTL activity by fd filamentous bacteriophages: role of CD4+ T cells in memory responses. J Biomed Biotechnol. 2010;2010:

SARTORIUS R, PISU P, **D'APICE L**, PIZZELLA L, ROMANO C, CORTESE G, GIORGINI A, SANTONI A, VELOTTI F, DE BERARDINIS P (2008). The use of filamentous bacteriophage fd to deliver MAGE-A10 or MAGE-A3 HLA-A2-restricted peptides and to induce strong antitumor CTL responses. JOURNAL OF IMMUNOLOGY, vol. 180(6); p. 3719-3728, ISSN: 0022-1767

D'APICE L., SARTORIUS R, CAIVANO A, MASCOLO D, DEL POZZO G, DI MASE DS, RICCA E, LI PIRA G, MANCA F, MALANGA D, DE PALMA R, DE BERARDINIS P (2007). Comparative analysis of new innovative vaccine formulations based on the use of procaryotic display systems. VACCINE, vol. 25(11); p. 1993-2000, ISSN: 0264-410X

LI PIRA G, BOTTONE L, IVALDI F, DEL GALDO F, PAPA F, ACCOLLA R, KOOPMAN G, ABBATE G, DE BERARDINIS P, **D'APICE L.**, DE PALMA R, MANCA F (2005). Human naive CD4 T-cell clones specific for HIV envelope persist for years in vivo in the absence of antigenic challenge. JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, vol. 40(2); p. 132-139, ISSN: 1525-4135

SARTORIUS R, **D'APICE L.**, BARBA P, GUARDIOLA J, SANTONI A, VELOTTI F, DE BERARDINIS P (2003). Induction of human NK cell-mediated cytotoxicity by CD40 triggering on antigen presenting cells. CELLULAR IMMUNOLOGY, vol. 221(2); p. 81-88, ISSN: 0008-8749

CAIVANO A, **D'APICE L.**, TIBERIO C, PRISCO A, ACUTO O, GUARDIOLA J, DE

BERARDINIS P (2001). Design of cassette vectors permitting cloning of all types of human TCR variable alpha and beta regions. JOURNAL OF IMMUNOLOGICAL METHODS, vol. 255(1); p. 125-134, ISSN: 0022-1759

D'APICE L., DE BERARDINIS P, PASQUINELLI R, CAPASSO I, D'AIUTO M, D'AIUTO G, ANZISI AM, FAVRE R, CERMOLA M, BARBA P, GUARDIOLA J (2000). Identification of a new subset of cells exhibiting dendritic phenotypes in patients affected by breast proliferative disorders. HUMAN IMMUNOLOGY, vol. 61(8); p. 739-752, ISSN: 0198-8859

DE BERARDINIS P, **D'APICE L.**, PRISCO A, OMBRA MN, BARBA P, DEL POZZO G, PETUKHOV S, MALIK P, PERHAM RN, GUARDIOLA J (1999). Recognition of HIV-derived B and T cell epitopes displayed on filamentous phages. VACCINE, vol. 17(11-12); p. 1434-1441, ISSN: 0264-410X

Since her apprenticeship at Institute of Protein Biochemistry, Luciana D'Apice has focused her interest on the study of the immune response. The aim of the study was the analysis of innovative vehicles for antigen delivery in order to produce new generation vaccines. She has analysed the immune response of T cell clones and lines derived from healthy donors against synthetic antigens derived from HIV-1 virus. The synthetic antigens were displayed in the context of recombinant proteins and filamentous bacteriophages.

The displaying of antigen on the coat of filamentous bacteriophage particles system was used also for effective peptide-based cancer vaccine development: using this vehicle in *in vitro* and *in vivo* systems she has demonstrated the efficacy of the vaccination by bacteriophages as strong CTL response and tumor protection.

In the context of the study of the cellular immune response she has faced the problem of the long term culture of cell clones and has developed a general approach based on a versatile cassette system, which allows cloning of all types of human T cell receptor alpha and beta variable region genes in expression vectors that can be easily transfected into immortalized cells, conferring the desired antigen specificity. The antigen specificity was measured as cytokines production and changing in the phosphorylation state of signaling molecules. The study of the activation signaling was performed during the year spent in the laboratory of molecular immunology of Pasteur Institute directed by dr. O. Acuto.

The immortalized cells reconstituted with the desired antigen specificity were also an useful tool in order to compare the antigenicity and immunogenicity of innovative delivery vehicles.

Her experience into T cell receptor reconstitution was useful to track T cell clones specific for HIV-1 antigens present in peripheral blood of seronegative, low risk donors and to assess the

presence of the same clone after a 15 year distance, due to long extended lifespan or homeostatic proliferation.

The long lasting experience in modifying the T cell receptor molecule has driven to the production and patenting of an engineered TCR able to block the mixed dimer formation, the most significant drawback in adoptive T cell therapy against cancer.

Since 2010 she is in charge for the flow cytometer facility shared by the IBP and IGB institutes and she uses the instrument to dissect the different populations involved into the immune response; by FACS analysis she was able to identify a new population subset present in the peripheral blood of women affected by breast disease, and to classify these cells as dendritic cells. Breast cancer was also the tumor lesion where the new isoform of a cross talk molecule was identified: the molecule Semaphorin6Ba was annotated and characterized in breast cancer cell lines and tissues derived from affected women. The breast cancer cell lines and tissues were also analyzed for the differential expression of adhesion molecules, and the results are summed up in the short report submitted to Molecular Carcinogenesis: Alternative splicing in genes encoding adhesion- and motility-related proteins in breast cancer" Rosanna Aversa, Anna Sorrentino, Roberta Esposito, Maria Rosaria Ambrosio, Angela Amato, Alberto Zambelli, Alfredo Ciccodicola, Luciana D'Apice, Valerio Costa.

Another cell population that she has studied are the natural killer cytotoxic cells, describing the role of cytokines as IL-15 and IL-12 and the surface receptor CD40 into the expansion of this cell population, opening new insight into the mechanism by which NK cells are activated in peripheral blood and giving useful hints for therapeutic application of anti-CD40 antibodies.

Actually she is improving the efficacy of the described antigenic vehicles displaying an antibody fragment that specifically target the delivered antigens to the professional antigen presenting dendritic cells, and exploiting the RNAseq potentiality she has described how the whole transcriptome of a professional Antigen Presenting Cell is modified when challenged with a proposed vaccine candidate, (Luciana D'Apice, Valerio Costa, Rossella Sartorius, Maria Trovato, Marianna Aprile and Piergiuseppe de Berardinis **Stimulation of innate and adaptive immunity by using filamentous bacteriophage fd targeted to DEC-205**. Journal Immunology research, under revision) (M. Trovato, F. Maurano, L D'Apice, V. Costa, R. Sartorius, F. Cuccaro, S. McBurney, S. J. Krebs, A. Ciccodicola, M. Rossi, N. L. Haigwood, A. Prisco, P. De Berardinis. **E2 multimeric scaffold for vaccine formulation: transcriptome analysis of pulsed dendritic cells and immune response by intranasal delivery**. BMC Medical Genomics submitted).

