

**FORMATO EUROPEO
PER IL CURRICULUM
VITAE**



INFORMAZIONI PERSONALI

Nome
Indirizzo
Telefono
Fax
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Nazionalità
Data di nascita

FEDERICO Maurizio

maurizio.federico@iss.it

Italiana

ESPERIENZA LAVORATIVA

• Date (da – a)

Agosto 2020-: Direttore f.f. del Centro Nazionale per la Salute Globale presso l'Istituto Superiore di Sanità (ISS), Roma.
Gennaio 2017- : Dirigente di Ricerca presso il Centro Nazionale per la Salute Globale ISS;
Marzo 2007: immissione in ruolo come Dirigente di Ricerca ISS;
Febbraio 2006-Dicembre 2016: Direttore del Reparto "Patogenesi dei Retrovirus" presso il Centro Nazionale AIDS, ISS;
Ottobre1992-Settembre 2005: Primo Ricercatore presso il Laboratorio di Malattie Infettive, Parassitarie ed Immunomediate, ISS;
Giugno 1985-Ottobre1992: Ricercatore di ruolo a tempo indeterminato presso il Laboratorio di Virologia, ISS;
Luglio 1982-Giugno 1985: Borsista presso il Laboratorio di Virologia, ISS.

ISTRUZIONE E FORMAZIONE

• Date (da – a)

Luglio 1982: Laurea in Scienze Biologiche presso l'Università La Sapienza. Votazione 110/110 con lode.

- Curriculum vitae di
FEDERICO Maurizio

Per ulteriori informazioni:
www.cedefop.eu.int/transparency
www.europa.eu.int/comm/education/index_it.html
www.eurescv-search.com

CAPACITÀ E COMPETENZE

PERSONALI

Acquisite nel corso della vita e della carriera ma non necessariamente riconosciute da certificati e diplomi ufficiali.

MADRELINGUA

ALTRE LINGUE

- Capacità di lettura
- Capacità di scrittura
- Capacità di espressione orale

CAPACITÀ E COMPETENZE

RELAZIONALI

Vivere e lavorare con altre persone, in ambiente multiculturale, occupando posti in cui la comunicazione è importante e in situazioni in cui è essenziale lavorare in squadra (ad es. cultura e sport), ecc.

Italiano

Inglese: Lettura: eccellente; Scrittura: eccellente; Capacità di espressione orale: eccellente

Francese: Lettura: Eccellente; Scrittura: buono; Capacità di espressione orale: buono

I primi 5 anni della carriera di ricercatore del dott. Maurizio Federico (MF) sono stati spesi studiando gli effetti antivirali/differenziazione degli interferoni di tipo I e II, nonché gli aspetti molecolari della differenziazione eritroide. Il successo di questa ricerca è testimoniato dalla inclusione nelle "authorship" di 9 articoli pubblicati su riviste internazionali peer-reviewed. Quelle più significative sono:

1. Romeo G., Affabris E., **Federico M.**, Mechti N., Coccia E.M., Jemma C., & Rossi G.B.

Establishment of the antiviral state in a/b interferon-resistant Friend cells treated with interferon: induction of 67K protein kinase activity in absence of detectable 2-5A synthetase. **J. Biol. Chem.** **1985**, 260: 3833-3.

2. **Federico M.**, Romeo G., Affabris E., Coccia E.M. & Rossi G.B.

2'-5'oligoadenylate synthetase-uninducible alpha/beta-interferon resistant Friend cells develop an antiviral state when permeabilized with lyssolecithin and treated with 2'-5' oligoadenylate oligomers. **J. Interferon Res.** **1986**, 6: 233-240.

3. Coccia E.M., **Federico M.**, Romeo G., Affabris E., Cofano F. & Rossi G.B.

Interferons α/β and γ -resistant Friend cells variants exhibiting receptor sites for interferons but no induction of 2-5A synthetase and 67K protein kinase. **J. Interferon Res.** **1988**, 8: 113-127.

4. Affabris E., **Federico M.**, Romeo G., Coccia E. & Rossi G.B.

Opposite effects of murine interferons on erythroid differentiation of Friend cells. **Virology.** **1988**, 167: 185-193.

La fine degli anni '80 sono stati gli anni dell'affermarsi dell'epidemia di AIDS in Italia. Nell'ambito del Laboratorio di Virologia del Ministero della Salute, MF ha collaborato con il team scientifico impegnato nell'isolamento e caratterizzazione degli isolati di HIV-1 circolanti in Italia. In questo contesto, MF ha contribuito in modo decisivo al primo isolamento, clonaggio molecolare e sequenziamento dell'HIV-1 da un malato italiano di AIDS. Da questo momento è iniziato un intenso lavoro focalizzato sugli aspetti sia molecolari che patogenetici della biologia dell'HIV-1. Il risultato più originale ottenuto da MF nel periodo in

questione è stato l'isolamento di un ceppo HIV-1 non produttore (HIV-1F12) la cui espressione inibisce fortemente la replicazione dell'HIV-1 superinfettante. Questa scoperta è stata oggetto di un brevetto in collaborazione con scienziati di MolMed, un'industria biotecnologica italiana di medie dimensioni, e i risultati sono stati descritti nei seguenti articoli pubblicati su riviste internazionali peer-reviewed leader nel campo della virologia:

1. **Federico M., Titti F., Buttò S., Orecchia A., Carlini F., Taddeo B., Macchi B., Maggiano N., Verani P., Rossi G.B.**
Biologic and molecular characterization of producer and nonproducer clones from HUT-78 cells infected with a patient HIV isolate. **AIDS Res Hum Retrovirol.** **1989.** 5: 385-395.
2. **Federico M., Taddeo B., Carlini F., Nappi F., Verani P., Rossi G.B.**
A recombinant retrovirus carrying a non-producer HIV-1 variant induces resistance to superinfecting HIV. **J Gen. Virol.** **1993.** 74: 2099-2110.
3. **Federico M., Taddeo B., Nappi F., Nicolini A., Rossi G.B., Verani P.**
Transfection of a retroviral construct carrying a non-producer HIV-1 variant induces HIV-1 resistance in CD4+ CEMss cells. **J. Biol Reg Homeost Ag.** **1993.** 7:41-49.
4. **Federico M., Nappi F., Bona R., d'Aloja P., Verani P., Rossi G.B.**
Full expression of transfected non-producer interfering HIV-1 proviral DNA abrogates susceptibility of human He-La CD4+ cells to HIV. **Virology.** **1995.** 206:76-84.

Alla fine degli anni '90, MF diventa responsabile di un team scientifico focalizzato sulla ricerca di base sull'HIV-1 presso il Laboratorio di Virologia dell'Istituto Superiore di Sanità. MF pubblica i primi articoli come autore senior su importanti riviste internazionali peer-reviewed. Il principale campo di interesse è stato lo studio delle funzioni della proteina HIV-1 Nef. A questo proposito, MF scopre un allele HIV-1 Nef unico in grado di trasformare il fenotipo di un HIV-1 infettivo in uno non produttore. Nel frattempo, MF avvia indagini anche nel campo delle tecnologie basate su vettori lentivirali.

- 1 **d'Aloja P., Olivetta E., Bona R., Nappi F., Pedacchia D., Pugliese K., Ferrari G., Verani P. and Federico M.**
Gag, Vif and Nef genes contribute to the homologous viral interference induced by a non-producer human immunodeficiency virus type-1 (HIV-I) variant: identification of novel HIV-1 inhibiting viral protein mutants. **J. Virol.** **1998,** 72,; 4308-4319.
2. **Federico M.**
Lentiviruses as gene delivery vectors. **Curr. Opin. Biotech.** **1999.** Vol.10, N.5, Oct., 448-453.
3. **Olivetta E., Pugliese K., Bona R., d'Aloja P., Ferrantelli F., Santarcangelo A.C., Mattia G., Verani P., and Federico**

M.

cis Expression of the F12 Human Immunodeficiency Virus (HIV) Nef allele transforms the highly productive NL4-3 HIV type 1 to a replication defective strain: involvement of both Env gp41 and CD4 intracytoplasmic tails. **J. Virol.** 2000, 74, 483-492.

4. *Fackler O.T., D'Aloja P., Baur A.S., **Federico M.**, and Peterlin B.M.*

Nef from Human Immunodeficiency Virus Type 1 F12 Inhibits viral production and infectivity. **J. Virol.** 2001, 75, 6601-6608.

In questo periodo MF ha ottenuto i primi finanziamenti per la ricerca come PI di progetti scientifici dedicati allo studio del ruolo di HIV-1 Nef nella patogenesi dell'AIDS, nonché allo sviluppo di nuove terapie anti-HIV basate sulla tecnologia del vettore lentivirale. Inoltre, MF ha ottenuto un secondo brevetto per lo sviluppo di un originale reagente anti-HIV basato sulla terapia genica. Nel frattempo, il team di cui fa parte MF e che è composto da 8-10 persone ha sviluppato una serie di importanti collaborazioni con gruppi scientifici nazionali e internazionali leader nel campo dell'HIV. Ad esempio, un grande sforzo collaborativo è stato sviluppato con il laboratorio diretto dal Prof. B.M. Peterlin, S. Francisco, California, USA, uno scienziato leader mondiale nella ricerca per l'HIV. Inoltre, un'intensa collaborazione con il Dr. A. Baur, Erlangen, Germania, ha prodotto importanti risultati sul ruolo dell'HIV-1 Nef nella patogenesi dell'AIDS. Le collaborazioni internazionali sono state fruttuose anche in termini di ottenimento di finanziamenti alla ricerca da parte della Comunità Europea. MF ha partecipato ai framework FP5 e FP6 come co-PI di progetti incentrati sulla biologia e l'inibizione terapeutica dell'HIV-1 Nef. Inoltre, a partire dal 1998, MF è stato PI di 14 proposte scientifiche approvate dal Programma Nazionale AIDS concesso dal Ministero della Salute italiano. Nel contesto delle indagini su Nef, MF ha scoperto e caratterizzato l'HIV-1 Nefmut che è parte fondamentale della originale piattaforma vaccinale CTL in seguito sviluppata ed ampliata.

1. *Peretti S, Schiavoni I, Pugliese K, Federico M.*
Cell Death Induced by the Herpes Simplex Virus-1 Thymidine Kinase Delivered by Human Immunodeficiency Virus-1-Based Virus-like Particles. *Mol Ther.* 2005 Dec;12(6):1185-1196.
2. *Peretti S, Schiavoni I, Pugliese K, Federico M.*
Selective elimination of HIV-1 infected cells by Env-directed, HIV-1 based Virus Like Particles. **Virology.** 2006, 345(1):115-126.
3. *Di Bonito P., Grasso F., Mochi S., Petrone L., Fanales-Belasio E., Mei A., Cesolini A., Laconi G., Conrad H., Bernhard H., Dembek C.J., Cosma A., Santini S.M., Lapenta C., Donati S., Muratori C., Giorgi C., **Federico M.***
Anti-tumor CD8+ cell immunity elicited by HIV-1 based Virus-Like Particles incorporating HPV-16 E7 protein. **Virology.** 2009. 395, 45-55.
4. *Di Bonito P, Ridolfi B, Columba-Cabezas S, Giovannelli A, Chiozzini C, Manfredi F, Anticoli S, Arenaccio C, **Federico M.*** HPV-E7 delivered by engineered exosomes elicits a protective CD8+ T cell-mediated immune response. **Viruses.**

2015, 7, 1079-1099.

Più recentemente, MF è stato anche coinvolto nello studio dell'interazione esosomi/HIV. In proposito, MF ha pubblicato dati che dimostrano la capacità di ADAM17 attivato caricato negli esosomi da cellule infette da HIV-1 di attivare linfociti T CD4+ primari quiescenti e HIV-1 latente.

1. Lee J.H. Wittki S., Brau T., Dreyer F.S., Kratzel K., Dindorf J., Johnston I.C.D., Gross S., Kremmer E., Zeidler R., Schlotzer-Schrehardt U., Lichtenheld M., Saksela K., Harrer T., Schuler G., **Federico M.**, Baur A.S.
HIV Nef-Associated Paxillin and Pak1/2 Regulate Activation and Secretion of TACE/ADAM10 Proteases, **Mol. Cell** 2013 49: 668-679.
2. Arenaccio C, Chiozzini C, Columba-Cabezas S, Manfredi F, **Federico M.**
Cell activation and HIV-1 replication in unstimulated CD4+ T lymphocytes ingesting exosomes from cells expressing defective HIV- **Retrovirology** 2014, 11:46.
3. Arenaccio C, Chiozzini C, Columba-Cabezas S, Manfredi F, Affabris E, Baur A, **Federico M.**
Exosomes from Human Immunodeficiency Virus Type 1 (HIV-1)-Infected Cells License Quiescent CD4+ T Lymphocytes To Replicate HIV-1 through a Nef- and ADAM17-Dependent Mechanism. **J. Virol.** 2014. 88:11529-11539.
4. Arenaccio C, Anticoli S, Manfredi F, Chiozzini C, Olivetta E, **Federico M.**
Latent HIV-1 is activated by exosomes from cells infected with either replication-competent or defective HIV-1 **Retrovirology** 2015 12, 87.

A questo proposito, il gruppo di ricerca di MF ha sviluppato un nuovo approccio per indurre l'immunità dei linfociti CD8+ T citotossici (CTL) basato sull'ingegnerizzazione in vivo di esosomi e, più in generale, di vescicole extracellulari (EV). Questo è un nuovo approccio alla vaccinazione che impiega un vettore di espressione del DNA che codifica per la proteina mutante HIV-1 Nefmut, un mutante che ha perso tutte le sue funzioni correlate alla patogenesi da HIV, mostrando nel contempo un'altissima efficienza di incorporazione nelle EV anche quando polipeptidi e proteine eterologhe vengono fuse al suo C-terminale. Grazie alla sua funzione di ancoraggio nelle EV, Nefmut è in grado di caricare grandi quantità di antigeni in EV prodotti spontaneamente da tutte le cellule, comprese quelle muscolari. Questa piattaforma di vaccini CTL si è già dimostrata in studi preclinici efficace contro i tumori derivati da HPV-16 e carcinomi mammari HER2 positivi, e si è dimostrata fortemente immunogenica contro un ampio numero di antigeni virali, tra cui VP24, VP40, Gp e NP del virus Ebola, NP del virus Flu-A, NP e Gc del CCHFV, NS3 del WNV, NS3 dell'HCV. La piattaforma di vaccini CTL basata su Nefmut è il risultato di 15 anni di sforzi nel campo delle EV/esosomi, come evidenziato da più di 20 articoli pubblicati su riviste internazionali peer-reviewed. Un brevetto che tutela l'uso industriale della nostra piattaforma è stato recentemente concesso dall'Ufficio Brevetti Europeo (EPO, Patent N. 3389701, Applicante: ISS, pubblicato nel Bollettino Europeo dei Brevetti 20/18 del

29/4/2020), e sono stati finanziati progetti focalizzati sul suo sviluppo. L'inizio del 2020 ha visto l'emergere della epidemia di COVID-19 (virus SARS-CoV-2). In proposito, MF ha intrapreso studi per applicare alla patologia SARS-CoV-2 la tecnologia vaccinale CTL precedentemente sviluppata in ISS, studi che hanno portato alla pubblicazione dei manoscritti qui sotto citati e all'applicazione di nuovi brevetti.

1. Anticoli S, Manfredi F, Chiozzini C, Arenaccio C, Olivetta E, Ferrantelli F, Capocefalo A, Falcone E, Ruggieri A, **Federico M.** An exosome-based vaccine platform imparts cytotoxic T lymphocyte immunity against viral antigens. **Biotechnology Journal**, 2018 Apr;13(4):e1700443. doi: 10.1002/biot.201700443. Epub 2018 Mar. 24. PubMed PMID: 29274250.
2. Anticoli S, Aricò E, Arenaccio C, Manfredi F, Chiozzini C, Olivetta E, Ferrantelli F, Lattanzi L, D'Urso MT, Proietti E, **Federico M.** Engineered exosomes emerging from muscle cells break immune tolerance to HER2 in transgenic mice and induce antigen-specific CTLs upon challenge by human dendritic cells **Journal of Molecular Medicine**. (Berl). 2018 Feb;96(2):211-221. doi: 10.1007/s00109-017-1617-2. Epub 2017 Dec 27. PMID: 29282521.
3. Ferrantelli F., Manfredi F., Chiozzini C., Anticoli S., Olivetta E., Arenaccio C., **Federico M.** DNA vectors generating engineered exosomes as novel CTL vaccine candidates against AIDS, hepatitis B, and tumors. **Molecular Biotechnology**, 2018. 60(11), 773-782. DOI: 10.1007/s12033-018-0114-3
4. Chiozzini C., Manfredi F., Arenaccio C., Ferrantelli F., Leone P., **Federico M.** N-Terminal Fatty Acids of NEF^{MUT} Are Required for the CD8⁺ T-Cell Immunogenicity of In Vivo Engineered Extracellular Vesicles. **Vaccines** 2020, 8, 243.
5. **Federico M.** The conundrum of current anti-SARS-CoV-2 vaccines. Cytokine Growth Factor Rev. 2021 Aug;60:46-51. doi: 10.1016/j.cytogfr.2021.03.001. Epub 2021 Mar 6. PMID: 33714693; PMCID: PMC7936752.
6. Ferrantelli F, Chiozzini C, Manfredi F, Giovannelli A, Leone P, **Federico M.** Simultaneous CD8⁺ T-Cell Immune Response against SARS-Cov-2 S, M, and N Induced by Endogenously Engineered Extracellular Vesicles in Both Spleen and Lungs. **Vaccines**. 2021 Mar 10;9(3):240. doi: 10.3390/vaccines9030240. PMID: 33801926.
7. Chiozzini C, Manfredi F, Ferrantelli F, Leone P, Giovannelli A, Olivetta E, **Federico M.** The C-Terminal Domain of Nef^{mut} Is Dispensable for the CD8⁺ T

Cell Immunogenicity of In Vivo Engineered Extracellular Vesicles. **Vaccines**. 2021 Apr 12;9(4):373. doi: 10.3390/vaccines9040373. PMID: 33921215; PMCID: PMC8068889.

8. *Ferrantelli F, Manfredi F, Chiozzini C, Leone P, Giovannelli A, Olivetta E, **Federico M***. Long-Term Antitumor CD8⁺ T Cell Immunity Induced by Endogenously Engineered Extracellular Vesicles. **Cancers** (Basel). 2021 May 8;13(9):2263. doi: 10.3390/cancers13092263. PMID: 34066801; PMCID: PMC8125873.
9. **Federico M**. Virus-Induced CD8⁺ T-Cell Immunity and Its Exploitation to Contain the SARS-CoV-2 Pandemic. **Vaccines**. 2021 Aug 18;9(8):922. doi: 10.3390/vaccines9080922. PMID: 34452047; PMCID: PMC8402519.
10. *Ferrantelli F, Chiozzini C, Manfredi F, Leone P, Spada M, Di Virgilio A, Giovannelli A, Sanchez M, Cara A, Michelinì Z, **Federico M***. Strong SARS-CoV-2 N-Specific CD8⁺ T Immunity Induced by Engineered Extracellular Vesicles Associates with Protection from Lethal Infection in Mice. **Viruses**. 2022 Feb 6;14(2):329. doi: 10.3390/v14020329. PMID: 35215922; PMCID: PMC8879411.
11. **Federico M**. Biological and Immune Responses to Current Anti-SARS-CoV-2 mRNA Vaccines beyond Anti-Spike Antibody Production. **J Immunol Res**. 2022 May 14;2022:4028577. doi: 10.1155/2022/4028577. PMID: 35607407; PMCID: PMC9124111.
12. *Manfredi F, Chiozzini C, Ferrantelli F, Leone P, Giovannelli A, Sanchez M, **Federico M***. Activation of Anti-SARS-CoV-2 Human CTLs by Extracellular Vesicles Engineered with the N Viral Protein. **Vaccines**. 2022 Jun 30;10(7):1060. doi: 10.3390/vaccines10071060. PMID: 35891224; PMCID: PMC9318727.
13. **Federico M**. How Do Anti-SARS-CoV-2 mRNA Vaccines Protect from Severe Disease? **Int J Mol Sci**. 2022 Sep 8;23(18):10374. doi: 10.3390/ijms231810374. PMID: 36142284; PMCID: PMC9499329.
14. *Manfredi F, Chiozzini C, Ferrantelli F, Leone P, Pugliese K, Spada M, Di Virgilio A, Giovannelli A, Valeri M, Cara A, Michelinì Z, Andreotti M, **Federico M***. Antiviral effect of SARS-CoV-2 N-specific CD8⁺ T cells induced in lungs by engineered extracellular vesicles. **NPJ Vaccines**. 2023 Jun 2;8(1):83. doi: 10.1038/s41541-023-00686-y. PMID: 37268624; PMCID: PMC10237059.
15. *Ferrantelli F, Manfredi F, Chiozzini C, Leone P, Pugliese K, Spada M, Di Virgilio A, Giovannelli A, Valeri M, Cara A, Michelinì*

Z, Andreotti M, **Federico M**, SARS-CoV-2-Specific CD8⁺ T-Cells in Blood but Not in the Lungs of Vaccinated K18-hACE2 Mice after Infection. **Vaccines**. 2023; 11(9):1433.
<https://doi.org/10.3390/vaccines11091433>

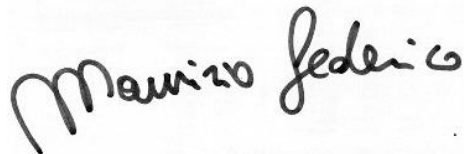
16. **Federico M**. The Immunologic Downsides Associated with the Powerful Translation of Current COVID-19 Vaccine mRNA Can Be Overcome by Mucosal Vaccines. **Vaccines (Basel)**. 2024 Nov 14;12(11):1281. doi: 10.3390/vaccines12111281. PMID: 39591184; PMCID: PMC11599006.

CAPACITÀ E COMPETENZE
ARTISTICHE
Musica, scrittura, disegno ecc.

Ha pubblicato il libro-denuncia. "Le Tre Vite di Lisa", Editore Armando.

Autorizzo il trattamento dei miei dati personali ai sensi del Decreto Legislativo 30 giugno 2003, n. 196 "Codice in materia di protezione dei dati personali". (facoltativo, v. istruzioni)

Firma



Finanziamenti degli ultimi 4 anni

- **MAECI (2019-2021)**
Anti-cancer immunotherapy through an innovative vaccine platform based on endogenously engineered exosomes.
Role: PI. € 165.000
- **BiovelocITA, Milan, Italy (2019-2020).**
An exosome-based vaccine platform for CTL immunity
Role: PI. € 540.000
- **RIPREI (2023-2025)**
An innovative anti-SARS-CoV-2 vaccine based on mucosal administration of extracellular vesicles incorporating the N viral antigen
Role: PI. € 310.000

In più, MF è stato PI di 8 progetti di ricerca nell'ambito del Programma Nazionale AIDS, nonché del Progetto per la Ricerca Finalizzata 2011, Ministero della Salute, n. 2308334 dal titolo "New therapeutics and immunogens generated by incorporating short RNAs and protein antigens in exosomes", importo € 451.500.

Elenco titoli:

- Lista pubblicazioni e brevetti;
- Lettera di nomina a Capo del Reparto “Patogenesi dei Retrovirus” afferente al Centro Nazionale AIDS, ISS;
- Lettera di nomina a Direttore f.f. del Centro Nazionale per la Salute Globale, ISS.

Europass Curriculum Vitae

The undersigned Dr. Maurizio Federico pursuant to art. 46 and 47 of Presidential Decree 445/2000, aware of the criminal sanctions provided for by art. 76 of Presidential Decree 445/2000 and subsequent amendments and additions for the cases of falsity in documents and false declarations, declares under his own responsibility

Personal information

First name(s) / Surname(s) **Maurizio Federico**

Address(es)

Telephone(s)

E-mail Maurizio.federico@iss.it

Nationality Italian

Date of birth

Dates August 2020-to date: Acting Director of the National Center for Global Health at the Istituto Superiore di Sanità (ISS), Rome

Occupation or position held January 2017-to date: Research Director at the National Center for Global Health ISS

Main activities and responsibilities March 2007: appointed as Research Director ISS

Name and address of employer February 2006-December 2016: Director of the "Pathogenesis of Retroviruses" Department at the National AIDS Center, ISS

Type of business or sector October 1992-September 2005: Senior Researcher at the Laboratory of Infectious, Parasitic and Immune-Mediated Diseases, ISS

June 1985-October 1992: Permanent Researcher at the Laboratory of Virology, ISS;

July 1982-June 1985: Scholarship holder at the Laboratory of Virology, ISS

Education

Dates July 1982: Degree in Biological Sciences at La Sapienza University. Grade 110/110 with honors.

Personal skills and competences

Mother tongue(s) Italian

English language English: Reading: Excellent; Writing: Excellent; Speaking: Excellent
French: Reading: Excellent; Writing: Good; Speaking: Good

Technical skills and competences

The first 5 years of Dr. Maurizio Federico's (MF) research career were spent studying the antiviral/differentiation effects of type I and II interferons, as well as the molecular aspects of erythroid differentiation. The success of this research is evidenced by the inclusion in the "authorship" of 9 articles published in international peer-reviewed journals. The most significant ones are:

1. Romeo G., Affabris E., Federico M., Mechti N., Coccia E.M., Jemma C., & Rossi G.B. Establishment of the antiviral state in a/b interferon-resistant Friend cells treated with interferon: induction of 67K protein kinase activity in absence of detectable 2-5A synthetase. *J. Biol. Chem.* 1985, 260: 3833-3.
2. Federico M., Romeo G., Affabris E., Coccia E.M. & Rossi G.B. 2'-5' oligoadenylate synthetase-uninducible alpha/beta-interferon resistant Friend cells develop an antiviral state when permeabilized with lysolecithin and treated with 2'-5' oligoadenylate oligomers. *J. Interferon Res.* 1986, 6: 233-240.
3. Coccia E.M., Federico M., Romeo G., Affabris E., Cofano F. & Rossi G.B. Interferons α/β and γ -resistant Friend cells variants exhibiting receptor sites for interferons but no induction of 2-5A synthetase and 67K protein kinase. *J. Interferon Res.* 1988, 8: 113-127.
4. Affabris E., Federico M., Romeo G., Coccia E. & Rossi G.B. Opposite effects of murine interferons on erythroid differentiation of Friend cells. *Virology.* 1988, 167: 185-193.

The late 1980s were the years of the emergence of the AIDS epidemic in Italy. Within the Laboratory of Virology of the Ministry of Health, MF collaborated with the scientific team engaged in the isolation and characterization of HIV-1 isolates circulating in Italy. In this context, MF contributed decisively to the first isolation, molecular cloning and sequencing of HIV-1 from an Italian AIDS patient. From this moment on, an intense work focused on both the molecular and pathogenetic aspects of HIV-1 biology began. The most original result obtained by MF in this period was the isolation of a non-producing HIV-1 strain (HIV-1F12) whose expression strongly inhibits the replication of superinfecting HIV-1. This discovery was the subject of a patent in collaboration with scientists from MolMed, a medium-sized Italian biotechnology company, and the results have been described in the following articles published in leading international peer-reviewed journals in the field of virology:

1. Federico M., Titti F., Buttò S., Orecchia A., Carlini F., Taddeo B., Macchi B., Maggiano N., Verani P., Rossi G.B. Biologic and molecular characterization of producer and nonproducer clones from HUT-78 cells infected with a patient HIV isolate. *AIDS Res Hum Retrovirol.* 1989, 5: 385-395.
2. Federico M., Taddeo B., Carlini F., Nappi F., Verani P., Rossi G.B. A recombinant retrovirus carrying a non-producer HIV-1 variant induces resistance to superinfecting HIV. *J Gen. Virol.* 1993, 74: 2099-2110.
3. Federico M., Taddeo B., Nappi F., Nicolini A., Rossi G.B., Verani P. Transfection of a retroviral construct carrying a non-producer HIV-1 variant induces HIV-1 resistance in CD4+ CEMss cells. *J. Biol Reg Homeost Ag.* 1993, 7:41-49.
4. Federico M., Nappi F., Bona R., d'Aloja P., Verani P., Rossi G.B. Full expression of transfected non-producer interfering HIV-1 proviral DNA abrogates susceptibility of human He-La CD4+ cells to HIV. *Virology.* 1995, 206:76-84.

In the late 1990s, MF became the leader of a scientific team focused on basic research on HIV-1 at the Laboratory of Virology of the Istituto Superiore di Sanità. MF published his first articles as senior author in important international peer-reviewed journals. His main field of interest was

the study of the functions of the HIV-1 Nef protein. In this regard, MF discovered a unique HIV-1 Nef allele capable of transforming the phenotype of an infectious HIV-1 into a non-producing one. In the meantime, MF also started investigations in the field of lentiviral vector-based technologies.

1 d'Aloja P., Olivetta E., Bona R., Nappi F., Pedacchia D, Pugliese K., Ferrari G., Verani P. and Federico M. Gag, Vif and Nef genes contribute to the homologous viral interference induced by a non-producer human immunodeficiency virus type-1 (HIV-1) variant: identification of novel HIV-1 inhibiting viral protein mutants. *J. Virol.* 1998, 72,; 4308-4319.

2. Federico M. Lentiviruses as gene delivery vectors. *Curr. Opin. Biotech.* 1999. Vol.10, N.5, Oct., 448-453.

3. Olivetta E., Pugliese K., Bona R., d'Aloja P., Ferrantelli, F., Santarcangelo A.C., Mattia G., Verani P., and Federico M. cis Expression of the F12 Human Immunodeficiency Virus (HIV) Nef allele transforms the highly productive NL4-3 HIV type 1 to a replication defective strain: involvement of both Env gp41 and CD4 intracytoplasmic tails. *J. Virol.* 2000, 74, 483-492.

4. Fackler O.T., D'Aloja P., Baur A.S., Federico M., and Peterlin B.M. Nef from Human Immunodeficiency Virus Type 1F12 Inhibits viral production and infectivity. *J. Virol.* 2001, 75, 6601-6608.

During this period MF obtained the first research funding as PI of scientific projects dedicated to the study of the role of HIV-1 Nef in the pathogenesis of AIDS, as well as to the development of new anti-HIV therapies based on lentiviral vector technology. In addition, MF obtained a second patent for the development of an original anti-HIV reagent based on gene therapy. In the meantime, the team of 8-10 people of which MF is a member has developed a number of important collaborations with leading national and international scientific groups in the HIV field. For example, a major collaborative effort has been developed with the laboratory directed by Prof. B.M. Peterlin, S. Francisco, California, USA, a world-leading scientist in HIV research. Furthermore, an intense collaboration with Dr. A. Baur, Erlangen, Germany, has produced important results on the role of HIV-1 Nef in the pathogenesis of AIDS. The international collaborations have also been fruitful in terms of obtaining research funding from the European Community. MF participated in the FP5 and FP6 frameworks as co-PI of projects focused on the biology and therapeutic inhibition of HIV-1 Nef. In addition, since 1998, MF has been PI of 14 scientific proposals approved by the National AIDS Program granted by the Italian Ministry of Health. In the context of the Nef investigations, MF discovered and characterized HIV-1 Nefmut which is a key part of the original CTL vaccine platform subsequently developed and expanded.

1. Peretti S, Schiavoni I, Pugliese K, Federico M. Cell Death Induced by the Herpes Simplex Virus-1 Thymidine Kinase Delivered by Human Immunodeficiency Virus-1-Based Virus-like Particles. *Mol Ther.* 2005 Dec;12(6):1185-1196.

2. Peretti S, Schiavoni I, Pugliese K, Federico M. Selective elimination of HIV-1 infected cells by Env-directed, HIV-1 based Virus Like Particles. *Virology.* 2006, 345(1):115-126.

3. Di Bonito P., Grasso F., Mochi S., Petrone L., Fanales-Belasio E., Mei A., Cesolini A., Laconi G., Conrad H., Bernhard H., Dembek C.J., Cosma A., Santini S.M., Lapenta C., Donati S., Muratori C., Giorgi C., Federico M. Anti-tumor CD8+ cell immunity elicited by HIV-1 based Virus-Like Particles incorporating HPV-16 E7 protein. *Virology.* 2009. 395, 45-55.

4. Di Bonito P, Ridolfi B, Columba-Cabezas S, Giovannelli A, Chiozzini C, Manfredi F, Anticoli S, Arenaccio C, Federico M. HPV-E7 delivered by engineered exosomes elicits a protective CD8+ T cell-mediated immune

response. *Viruses*. 2015, 7, 1079-1099.

More recently, MF has also been involved in the study of exosome/HIV interaction. In this regard, MF has published data demonstrating the ability of activated ADAM17 loaded in exosomes from HIV-1 infected cells to activate quiescent primary CD4+ T cells and latent HIV-1.

1. Lee J.H. Wittki S., Brau T., Dreyer F.S., Kratzel K., Dindorf J., Johnston I.C.D., Gross S., Kremmer E., Zeidler R., Schlotzer-Schrehardt U., Lichtenheld M., Saksela K., Harrer T., Schuler G., Federico M., Baur A.S.. HIV Nef-Associated Paxillin and Pak1/2 Regulate Activation and Secretion of TACE/ADAM10 Proteases, *Mol. Cell* 2013 49: 668-679.

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4. Arenaccio C, Anticoli S, Manfredi F, Chiozzini C, Olivetta E, Federico M. Latent HIV-1 is activated by exosomes from cells infected with either replication-competent or defective HIV-1 *Retrovirology* 2015 12, 87.

In this regard, the MF research group has developed a novel approach to induce CD8+ cytotoxic T lymphocyte (CTL) immunity based on the in vivo engineering of exosomes and, more generally, extracellular vesicles (EVs). This is a novel vaccination approach that employs a DNA expression vector encoding the HIV-1 mutant protein Nefmut, a mutant that has lost all its functions related to HIV pathogenesis, while showing a very high efficiency of incorporation into EVs even when heterologous polypeptides and proteins are fused to its C-terminus. Thanks to its EV-anchoring function, Nefmut is able to load large amounts of antigens into EVs spontaneously produced by all cells, including muscle cells. This CTL vaccine platform has already been shown in preclinical studies to be effective against HPV-16-derived tumors and HER2-positive breast cancers, and has been shown to be highly immunogenic against a large number of viral antigens, including VP24, VP40, Ebola virus Gp and NP, Flu-A virus NP, CCHFV NP and Gc, WNV NS3, HCV NS3. The Nefmut-based CTL vaccine platform is the result of 15 years of efforts in the EV/exosome field, as evidenced by more than 20 articles published in international peer-reviewed journals. A patent covering the industrial use of our platform has recently been granted by the European Patent Office (EPO, Patent No. 3389701, Applicant: ISS, published in the European Patent Bulletin 20/18 of 29/4/2020), and projects focused on its development have been funded. The beginning of 2020 saw the emergence of the COVID-19 (SARS-CoV-2) epidemic. In this regard, MF has undertaken studies to apply the CTL vaccine technology previously developed in ISS to the SARS-CoV-2 pathology, studies that have led to the publication of the manuscripts cited below and to the application of new patents.

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2. Anticoli S, Aricò E, Arenaccio C, Manfredi F, Chiozzini C, Olivetta E, Ferrantelli F, Lattanzi L, D'Urso MT, Proietti E, Federico M. Engineered

- exosomes emerging from muscle cells break immune tolerance to HER2 intratransgenic mice and induce antigen-specific CTLs upon challenge by human dendritic cells *Journal of Molecular Medicine*. (Berl). 2018 Feb;96(2):211-221. doi: 10.1007/s00109-017-1617-2. Epub 2017 Dec 27. PMID: 29282521.
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 6. Ferrantelli F, Chiozzini C, Manfredi F, Giovannelli A, Leone P, Federico M. Simultaneous CD8+ T-Cell Immune Response against SARS-CoV-2 S, M, and N Induced by Endogenously Engineered Extracellular Vesicles in Both Spleen and Lungs. *Vaccines*. 2021 Mar 10;9(3):240. doi: 10.3390/vaccines9030240. PMID: 33801926.
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 12. Manfredi F, Chiozzini C, Ferrantelli F, Leone P, Giovannelli A, Sanchez M, Federico M. Activation of Anti-SARS-CoV-2 Human CTLs by Extracellular Vesicles Engineered with the N Viral Protein. *Vaccines*. 2022 Jun 30;10(7):1060. doi: 10.3390/vaccines10071060. PMID: 35891224; PMCID: PMC9318727.
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16. Federico M. The Immunologic Downsides Associated with the Powerful Translation of Current COVID-19 Vaccine mRNA Can Be Overcome by Mucosal Vaccines. Vaccines (Basel). 2024 Nov 14;12(11):1281. doi: 10.3390/vaccines12111281. PMID: 39591184; PMCID: PMC11599006.

Computer skills and competences
ARTISTIC SKILLS AND COMPETENCES

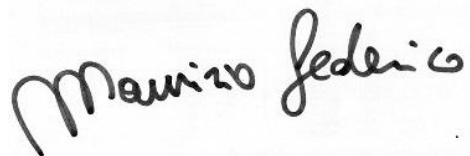
Familiarity with the entire Windows 365 package as well as the most popular graphics software
He published the book-denunciation. "Le Tre Vite di Lisa", Armando Publisher.

I authorize the processing of my personal data in accordance with Legislative Decree 30 June 2003, n. 196 "Code regarding the protection of personal data".

The personal data collected will be treated in accordance with the principles and provisions of Legislative Decree no. 196/2003 regarding the protection of confidentiality and then only for the purpose of managing the competition procedure.

Date, 15-01-2025

Signature



Funding in the last 4 years

• **MAECI** (2019-2021)

Anti-cancer immunotherapy through an innovative vaccine platform based on endogenously engineered exosomes.

Role: PI. € 165,000

• **BiovelocITA**, Milan, Italy (2019-2020).

An exosome-based vaccine platform for CTL immunity

Role: PI. € 540,000

• **RIPREI** (2023-2025)

An innovative anti-SARS-CoV-2 vaccine based on mucosal administration of extracellular vesicles incorporating the N viral antigen
Role: PI. € 310,000

In addition, MF has been PI of 8 research projects within the National AIDS Program and the Project for Finalized Research 2011, Ministry of Health, n. 2308334 entitled "New therapeutics and immunogens generated by incorporating short RNAs and protein antigens in exosomes", amount € 451,500.

List of titles:

- List of publications and patents;
- Letter of appointment as Head of the Department "Pathogenesis of Retroviruses" at the National AIDS Center, ISS;
- Letter of appointment as Acting Director of the National Center for Global Health, ISS.

ELENCO DI:

LIBRI –PROGETTI DI RICERCA RECENTI – PUBBLICAZIONI SCIENTIFICHE “PEER-REVIEWED”- BREVETTI

Dott. Maurizio FEDERICO

MF è stato editore dei seguenti libri:

1. Lentivirus Gene Engineering Protocols.
Methods in Molecular Biology, vol. 299, **M. Federico** Editor, Humana Press, Springer Science, New York, 2003.
2. Lentivirus Gene Engineering Protocols, Second Edition.
Methods in Molecular Biology, vol. 614, **M. Federico** Editor, Springer Science, New York, 2010
3. Lentiviral Vectors and Exosomes as Gene and Protein Delivery Tools.
Methods in Molecular Biology, vol. 1448, **M. Federico** Editor, Springer Science, New York, 2016.
4. Extracellular vesicles in diagnosis and therapy. B. Ridolfi & **M. Federico** Editors, *Methods in Molecular Biology*, Springer Science, New York, 2023.

MF è stato “Guest Editor” per due volumi della rivista scientifica “Current Drug Targets” nel 2004 e nel 2014.

MF ha agito come reviewer di più di 70 manoscritti e progetti scientifici.
MF ha depositato 5 brevetti in qualità di inventore.

La lista completa delle pubblicazioni di MF è riportata in

ORCID ID: 0000-0003-4154-1025

Scopus Author id: 56519363800

Research ID: J-5867-2016

H index: 35 (source: ResearchGate, <https://www.researchgate.net/profile/Maurizio-Federico>)

Selected Publication list of dr. Maurizio FEDERICO

Publications on Books

1. Rossi G.B., Pulciani S., e **Federico M.**
The molecular biology of retroviruses.
"The Molecular basis of Viral Replication", R. Perez
Bercoff (Ed.), NATO ASI Series, Vol. 136, Plenum Press, pp. 355-414, 1987.
2. **M. Federico**
From lentiviruses to lentivirus vectors.
Methods Mol Biol. 2003;229:3-15. doi: 10.1385/1-59259-393-3:3. PMID: 12824617
3. **M. Federico**
The outstanding role of Nef in the response of macrophage to HIV infection
In “HIV and the macrophage” Editor G. Herbein. 2007. Transworld Research Network

Proceedings

1. Jemma C., Palladino P., **Federico M.**, Rossi G.B.
Interferone e sistema immunitario. "Aggiornamenti su malattie infettive ed immunologia".
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2. **Federico M.**, Affabris E., Romeo G., Jemma C., Palladino P., Rossi G.B.
Cellule di Friend resistenti all'interferone alfa/beta sviluppano uno stato antivirale in seguito al trattamento con interferone gamma.
In "Società Italiana di Chemioterapia - XIII Congresso Nazionale", Catania 9-11 giugno 1983, 2, pp.275-276, 1983
3. Romeo G., Affabris E., **Federico M.**, Jemma C., Belardelli F., Mechti N., Gresser I. & Rossi G.B.
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Metodiche di rilevazione, con esemplificazione relative al virus di Friend.
In "Colture cellulari: tecniche di base ed applicazioni in oncologia" R. Sitia ed., Segreteria Gruppo Cooperazione in Immunologia: 51-67, 1984
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7. Rossi G.B., Affabris E., Romeo G., **Federico M.**, Coccia E.M., Mechti N., Lebleu B.
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In "The 2-5A System: Molecular and Clinical Aspects of the Interferon-regulated Pathway", B. Williams and R. Silverman eds., Alan Liss Inc., New York, NY 202, pp. 285-296, 1985.
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Ippolito G. & Manzari V.
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12. **Federico M.**, Macchi B., Orecchia A., Butt_ S., Verani P. & G.B. Rossi.
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"Consiglio Nazionale delle ricerche: progetto finalizzato per il controllo delle malattie da i infezione" 1987
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of Friend cells.
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Interferon modulatori of growth and differentiation of Friend erythroleukemia cells.
"The Status of Differentiation Therapy on Cancer, S. Waxman, G.B. Rossi & F. Takaku (Eds.), Serono
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Identificazione dei determinanti genetici responsabili del fenotipo non produttore di un clone di HIV-1(F12) mediante studi di complementazione
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BREVETTI

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Title: *Composition and Method of Imparting Resistivity to HIV Superinfection to Cells*
(PCT, N. PCT/IT96/00185, October 8 1996; Publication N. WO97/13861, April 17 1997)

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(United Kingdom patent application N. 0221778.4, priority date September 19 2002, abandoned;
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Domanda numero: 102016000101794
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Title: Nucleotide sequence expressing exosome-anchoring protein for use in immunotherapy
Sequenza nucleotidica esprime una proteina ancorante esosomi per uso come vaccino
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Nucleotide sequence expressing an exosome-anchoring protein for use as vaccine"

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